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Doctor's Dissertation

The Peroxyacetic Acid Oxidation of 4-Methylphenols and Their Methyl Ethers

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THE PEROXYACETIC ACID OXIDATION OF 4-METHYLPHENOLS AND THEIR METHYL ETHERS

A thesis submitted by

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SUMMARY

The peroxyacetic acid oxidation of 4-methylphenols and their methyl ethers in aqueous acetic acid at 25° was investigated using a 3:1 molar ratio of peroxyacid to substrate. Reaction products and oxidation stoichiometry (moles peroxyacid consumed to moles substrate consumed) were determined. Gas chromatography was used for qualitative and quantitative product analysis. Carboxylic acid products were converted to methyl and trimethylsilyl esters to permit their analysis. Every significant product detected by gas-liquid chromatography was collected and identified as were isolated precipitates. Structure assignments were made on the basis of infrared, NMR, and mass spectral analyses. In general, about one-half of the total theoretical product was accounted for.

Peroxyacetic acid oxidation of 4-methylpyrocatechol resulted solely in ring cleavage: β-methylmuconic acid (2%) was formed in addition to the corresponding β-methyl- and γ-methyl-γ-lactone acids (35 and 4%, respectively). These three products will be referred to collectively as "muconic acids." γ-Carboxymethyl-γ-hydroxy-β-methyl-$\Delta^{\alpha,\beta}$-butyrolactone (hydroxylactone, 5%) was also a reaction product. These products were unreactive with peroxyacetic acid under the reaction conditions. The reaction stoichiometry was 2.1, in agreement with the theoretical requirements of the detected products.

The oxidation of 2-methoxy-p-cresol gave a lower yield of muconic acids (20%) but a much higher yield of hydroxylactone (13%). The reaction stoichiometry of 3.0 was much higher than could be explained by the identified products. The oxidation of 4-methylveratrole gave 2-methoxy-5-methyl-p-benzoquinone (17%)

in addition to the muconic acids (13%) and hydroxylactone (1%). This reaction also gave a stoichiometry (2.9) that was higher than predicted. It was found that secondary oxidation of the p-quinone product occurred.

p-Cresol was oxidized to muconic acids (33%), hydroxylactone (4%), and 4-hydroxy-4-methyl-2,5-cyclohexadienone (12%). The reaction stoichiometry of 2.6 was in agreement with the products formed. The reaction was unaffected by methyl methacrylate which excluded the possibility of a free radical mechanism.

The oxidation of p-methylanisole gave muconic acids (15%), hydroxylactone (2%), 4-hydroxy-4-methyl-2,5-cyclohexadienone (16%), and 2-methoxy-5-methyl-p-benzoquinone (15%). The reaction stoichiometry (3.0) was consistent with the products formed and the reactivity of the p-quinone.

The approximate half-lives (hours) of the substrates studied were as follows: 4-methyl-o-benzoquinone (0.01); 4-methylpyrocatechol (0.2); 2-methoxy-p-cresol (4); 4-methylveratrole (5); p-cresol (25); p-methylanisole (100).

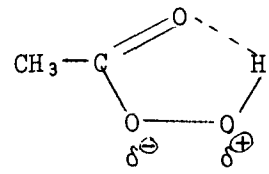
Initial hydroxylation of p-cresol and p-methylanisole by peroxyacetic acid took place at positions ortho and para to the original oxygen-containing substituent. Ortho-hydroxylation of p-methylanisole gave 2-hydroxy-p-methylanisole (which was isolated); p-cresol presumably gave 4-methylpyrocatechol which was oxidized too readily to survive. Oxidation of 4-methyl-o-benzoquinone gave the same distribution of muconic acid products found from all other oxidations; this strongly supports oxidation of 1,2-dioxy systems to muconic acids via the proposed o-quinone intermediate. Hydroxylation of the 1,2-dioxy

intermediate at the C-5 position on the ring evidently leads to formation of the p-quinone and hydroxylactone products. Thus, it was possible to construct one oxidation sequence that accounted for all of the products found from the various substrate oxidations.

INTRODUCTION

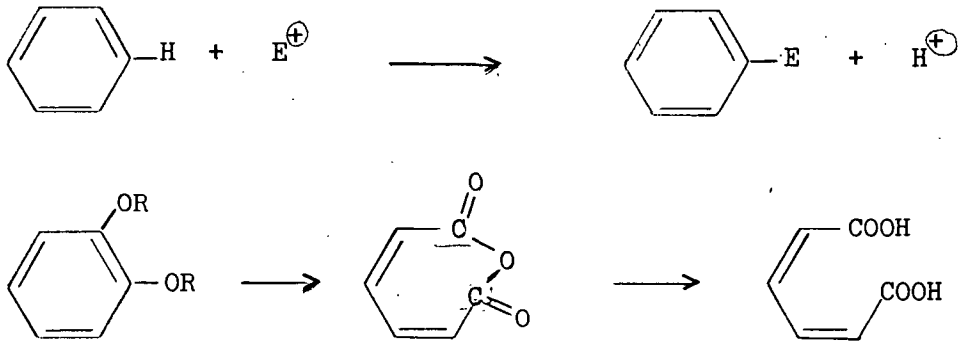
The chemical reactivity of both peroxyacids and hydrogen peroxide is a result of the weakness of the peroxide covalent bond. In peroxyacids, the peroxide bond is further weakened by the electrical dissymmetry caused by the acyl substituent. This weak bond, therefore, is the driving force in peroxyacid oxidations (1). As a result, a peroxyacid tends to stabilize itself as a carboxylate anion, apparently donating a cationic hydroxyl residue, $(OH)^+$. Hydroxyl cations, however, have never been detected as separate entities. Thus, peroxyacids may be thought of as electrophilic reagents.

Peroxyacetic acid, one of the more commonly used peroxyacids, is very strongly hydrogen bonded in solution, even more so than acetic acid. This results in formation of a particularly stable five-membered ring (2, 3), which is apparently the reason the pKa of peroxyacetic acid is so much higher than that of acetic acid (8.2 and 4.76, respectively).



Due to the tendency to lose a hydroxyl cation, the outer peroxy oxygen must possess a partial positive charge. This outer oxygen could then be thought of as the attacking point of a peroxyacetic acid molecule which would seek out electron-rich sites.

This thesis will be primarily concerned with reactions involving electrophilic attack of aromatic structures. A benzene ring is quite susceptible to electrophilic attack because of its cloud of π-electrons. With peroxyacids, the attack can result in substitution or cleavage of a carbon-carbon bond:



Substituents on the benzene ring can have a very great effect on both the reaction rate and the type of reaction that takes place. The effects of the electronic character of these groups are well known (4, 5).

PEROXYACID OXIDATION REACTIONS

Peroxyacetic acid, the electrophile of interest in this study decomposes along several routes, all subject to catalysis by metal ions. Products include acetic acid and either hydrogen peroxide or oxygen (6).

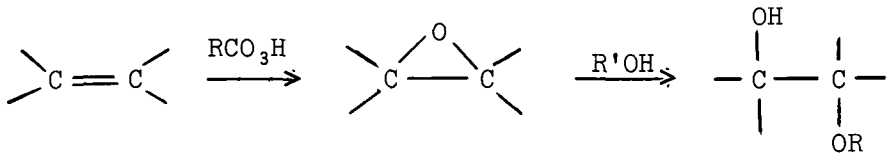
$$CH_3CO_3H + H_2O \rightleftarrows CH_3CO_2H + H_2O_2$$

$$2CH_3CO_3H \rightleftarrows 2CH_3CO_2H + O_2$$

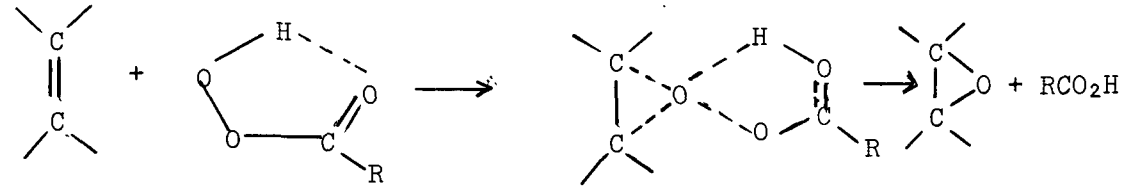
Conversely, peroxyacetic acid is commonly prepared by the oxidation of acetic acid with hydrogen peroxide in the presence of sulfuric acid as a catalyst.

Several reviews have been published on peroxyacid and hydrogen peroxide reactions (7-9) illustrating the oxidations of olefin and carbonyl groups and aromatic compounds.

Peroxyacid oxidation of carbon-carbon double bonds is well known. The initial product in this reaction is an epoxide, which opens in hydroxyl-containing solvents to form a product with one or two hydroxyl groups (10, 11). Peroxyacetic acid in

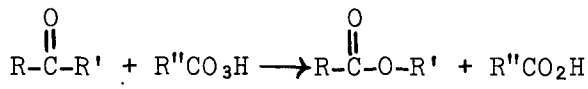


aqueous solution is very efficient in hydroxylating double bonds. Initial reaction is thought to proceed by attack of the outer peroxy oxygen to give the epoxide:

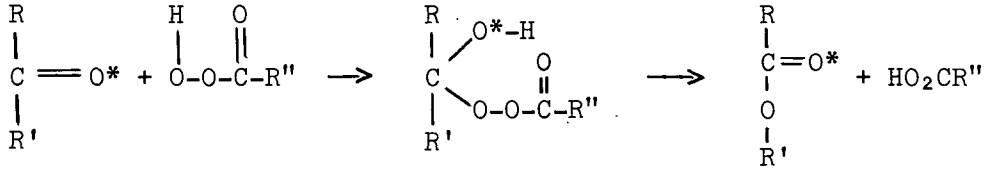


In all peroxyacid oxidations, any decrease in electron density at the point of attack, the double bond in this case, will result in a decrease in reactivity toward a peroxyacid. Therefore, conjugation of the olefin group with a carbonyl group or another olefin group will result in a slower reaction. Conversely, neighboring electron-releasing groups such as methyl or phenyl accelerate the reaction (10, 11).

The reactions of ketones with peroxyacids have undergone considerable study, and Hassall (12) has written a summary of these reactions. These oxidations are referred to as Baeyer-Villiger oxidations (13) and result in insertion of an oxygen atom between the carbonyl carbon and an adjacent group.

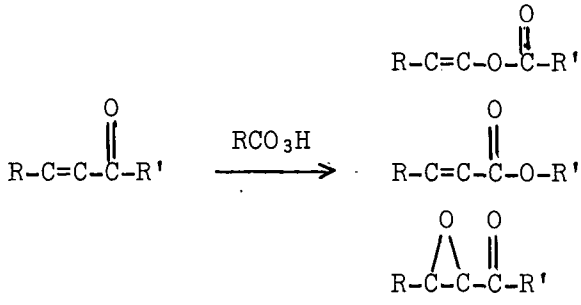


Several workers have studied the relative migratory ability of various groups and have shown that the predominant migrating group is the one best able to stabilize a positive charge; i.e., having the most electron-releasing character (14, 15). Criegee (16) showed that the final ester carbonyl oxygen is the same one present in the original ketone and proposed the following mechanism which is still generally accepted (17):

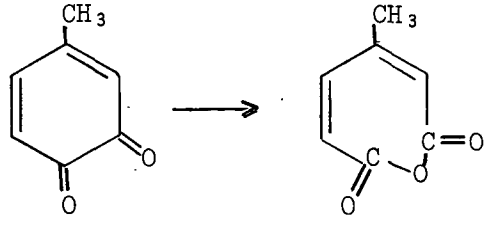


Aldehydes usually react with peroxyacids to form the corresponding carboxylic acid (9).

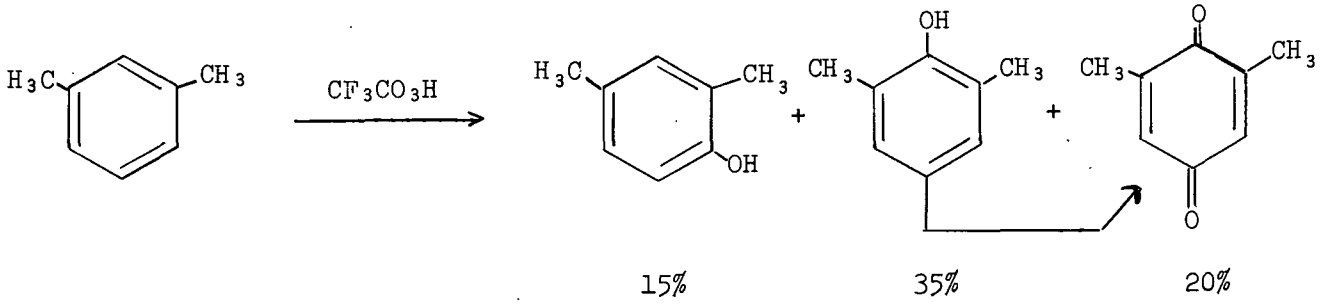
As mentioned in the case of olefins, conjugation with a double bond will slow or in some cases stop the oxidation. However, when reaction does occur, an α,β-unsaturated ketone yields several products (18):



α-Dicarbonyl compounds have been studied to a limited extent. Two different groups of workers (19, 20) oxidized 4-methyl-o-benzoquinone with monoperoxyphthalic acid and isolated the anhydride in an organic solvent.

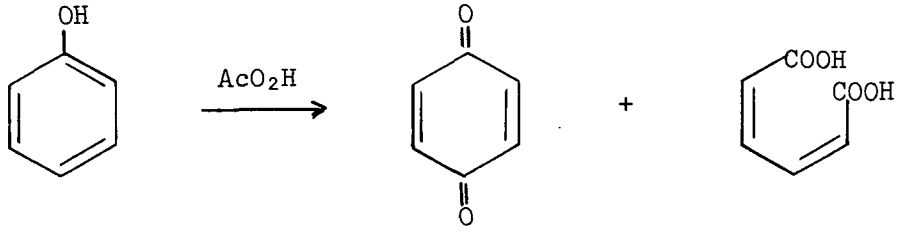


The peroxyacid oxidation of aromatic compounds, of greatest interest to this thesis, generally proceeds in three ways: hydroxylation of the aromatic ring, quinone formation, or ring cleavage to diacids. Simple hydroxylation has been noted in the literature in only a few cases. Chambers and coworkers (21) found that m-xylene is hydroxylated by trifluoroperoxyacetic acid to 2,4- and 2,6-xylenol with a p-quinone evidently resulting from further oxidation of 2,6-xylenol. The reason few hydroxylation reactions with peroxyacids have been noted is probably because a



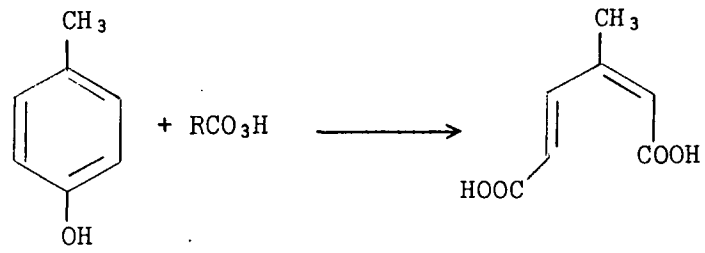
newly hydroxylated aromatic compound is often more reactive than the starting material and is oxidized further to other products.

Phenol is a good example of how a hydroxyl-containing aromatic ring can react when not blocked by alkyl groups. Many studies have been published on the oxidation of phenol by peroxyacetic acid (22-24) showing the formation of p-benzoquinone and muconic acid:



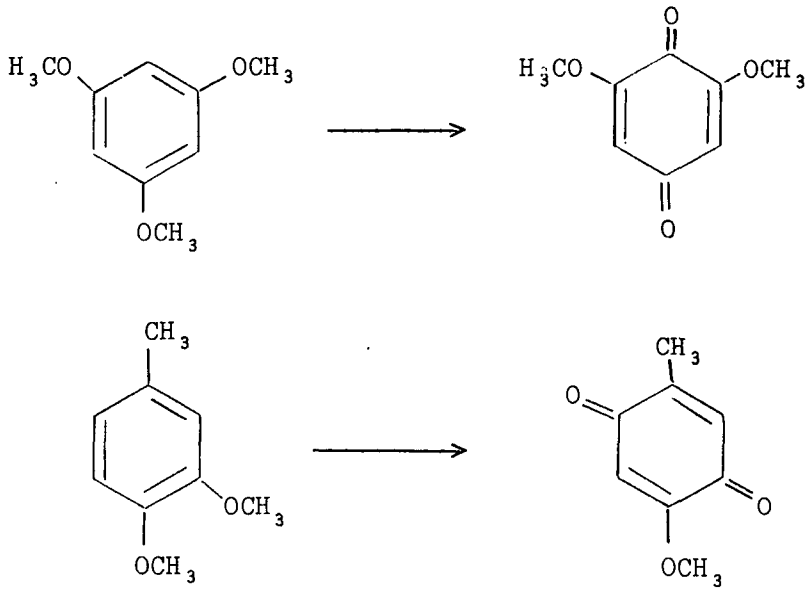
However, the placement of methyl groups on the aromatic ring can prevent one or the other of the above products from forming. Substitution para to the hydroxyl as in p-cresol apparently prohibits p-quinone formation and only cis,trans-β-methylmuconic

acid has been found (22, 25). In a similar way, only the p-quinone is found when



methyl groups are positioned ortho to the hydroxyl group. The methyl groups evidently prevent oxidation to a muconic acid (21, 26). From these results, it appears that methyl groups are unaffected by peroxyacids, but their presence can change the course of the reaction.

Phenyl ethers react slower than the corresponding free phenols and yield primarily p-quinones as products (27, 28). It was found that methoxyl groups were easily lost to enable formation of a p-quinone. The discovery was also made that, in general, the more methoxyl groups present on the ring, the more reactive the ring was toward peroxyacid attack.

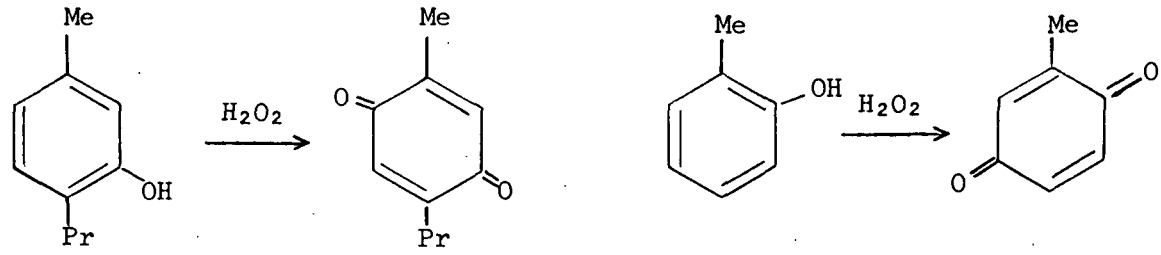


Very few examples of ring cleavage have been found in peroxyacid oxidations of aromatic ethers. Friess and coworkers (27) found that peroxybenzoic acid (PB) oxidized veratrole to dimethylmuconate. Some naphthalene methyl ethers also gave ring cleavage products when oxidized by peroxybenzoic acid (29, 30). Ibne-Rasa and Edwards (31) studied the peroxyacetic acid oxidation of some aromatic amines in the presence of methylmethacrylate, an excellent radical trap, and found no change in the rate of reaction. Since methylmethacrylate would consume any free radicals present, a change in reaction rate would probably have occurred had this oxidation been free radical. Although this is a different reaction than the aromatic oxidations studied in this thesis, it may indicate that noncatalyzed peroxyacid oxidations are not free radical.

HYDROGEN PEROXIDE OXIDATION REACTIONS

The reactions of hydrogen peroxide with organic compounds are also of interest in this study because some hydrogen peroxide is always present in peroxyacetic acid solutions. Hydrogen peroxide can react in many of the same ways as peroxyacids, but these reactions usually involve either alkaline hydrogen peroxide or use of metal catalysts (7, 32). The reactions of hydrogen peroxide with organic compounds in slightly acidic systems are limited. Acid or neutral hydrogen peroxide is not as effective as peroxyacids in hydroxylation, although it will react slowly with some double bonds (7). Ketones are not usually oxidized by acidic hydrogen peroxide although α-dicarbonyl compounds are oxidized to the acid anhydride (33, 34).

Aromatic oxidations by hydrogen peroxide evidently are limited to phenols under acid conditions. Henderson and Boyd (35) found that some alkyl phenols were oxidized to p-quinones by 30% aqueous hydrogen peroxide. However, anisole will not react with



hydrogen peroxide unless a metal catalyst is present (36).

PEROXYACETIC ACID IN PULPING AND BLEACHING

All of these reactions demonstrate the versatility of a peroxyacid as a result of its ability to react with several different types of chemical groups. It was probably for this reason that peroxyacetic acid was first investigated as a possible pulping and bleaching chemical for use in the pulp and paper industry. The main purpose of pulping and bleaching reactions is the removal of lignin from the wood. Since lignin is known to contain olefin groups, carbonyl groups, and phenolic structures, all of which have been shown to be oxidized by peroxyacids, it would seem likely that an oxidant such as peroxyacetic acid would be a suitable delignifying agent.

Another point in its favor is that peroxyacetic acid does not react to any large extent with the carbohydrates in wood. Many workers (37-41) have studied the effect of peroxyacetic acid on wood pulps and other cellulosic fibers and found the carbohydrate fraction to remain relatively intact. Peroxyacetic acid has been compared favorably with chlorine dioxide and other oxidants in producing holocellulose pulps.

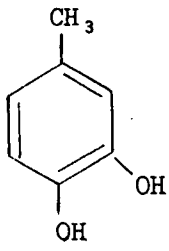
Although there is general agreement that peroxyacetic acid selectively removes lignin from wood, it is not known exactly how the lignin is oxidized. Ishikawa and coworkers (42, 43) found muconic acid derivatives after peroxyacetic acid oxidation of wood and isolated lignins, indicating ring cleavage and demethoxylation. They also found carboxyl formation on side chains. This all resulted in degradation of the lignin molecule to water-soluble lower molecular weight fragments. A study by Sarkanen and Suzuki (44) gave the same results, concluding that the predominant reaction was ring opening to give muconic acid structures. In a more recent paper coauthored by Sarkanen (45), it was proposed that from one third to one fourth of the aromatic nuclei remained unchanged.

However, in one case (46) a high yield (80-90%) of water-soluble aromatic compounds of low molecular weight was reported.

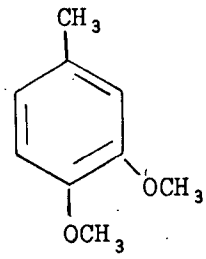
PROPOSED STUDY

After reviewing the literature, it is evident that there is little comprehensive information on the peroxyacid oxidation of aromatic compounds. Up to now, no detailed study of the products, product yields, and stoichiometry of even one aromatic oxidation by a peroxyacid has been published to my knowledge. It was for this reason and because of its possibilities as a pulping and bleaching agent that the reactions of peroxyacetic acid were studied.

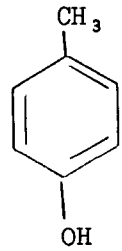
Since the basic reactions of the aromatic ring have not been fully investigated to date, it was felt inappropriate at this time to study somewhat complex molecules that would be closely related to lignin. Therefore, the main compounds studied were 4-methylpyrocatechol (I), 4-methylveratrole (II), p-cresol (III), and p-methylanisole (IV).



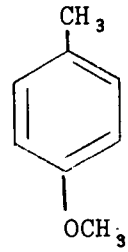
I



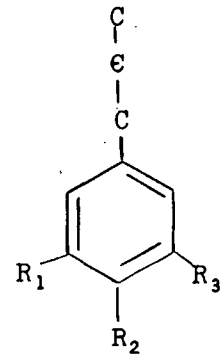
II



III



IV



V

R_1, R_2, R_3 = H, OH, or OCH_3

Some of the structural units (V) present in lignin are similar to these compounds. Also, the presence of hydroxyl and methoxyl groups on the ring should offer useful information concerning the relative reactivity of these two groups and how they affect the course of the reaction. A thorough study of this family of compounds will lay a foundation for further work with more complex molecules more closely related to lignin and should also give some immediate information concerning possible lignin reactions with peroxyacetic acid.

RESULTS AND DISCUSSION

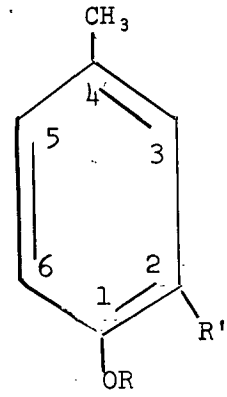
GENERAL OXIDATION CONDITIONS AND ANALYSIS PROCEDURES

All substrates (12 mmoles) in the following oxidations were mixed with 10% peroxyacetic acid (36 mmoles) and run at 25°. The hydrogen peroxide concentration in the peroxyacetic acid solutions was generally kept below 0.3% by using the peroxyacid while still fresh. At the end of the reaction, the oxidation solutions were mixed with acetaldehyde to reduce any remaining peroxyacetic acid. This product solution was subsequently mixed with sodium carbonate to neutralize the acetic acid and carboxylic acid products and was then extracted with ether. This initial ether extract contained all of the neutral (noncarboxylic) products. The remaining alkaline layer was acidified and worked up to isolate the carboxylic acid products. This is all reported in the experimental section and was carried out on all products except where noted otherwise.

All products isolated from the various oxidations were examined by infrared, and this information was enough for positive identification when the known infrared was available. For the other main products, both NMR and mass spectra were determined. Carbon-hydrogen analyses were not run because it would have been very difficult to get a sufficient quantity of the products absolutely pure. It was felt that data from infrared, NMR, and mass spectra were sufficient to give an accurate identification of these relatively simple products.

The GLC method used in this study generally accounted for one-half of the products. Other analytical methods such as paper, thin layer, or column chromatography would probably have been necessary to detect the other products. This thesis was restricted to the products that could be found by gas chromatography or by precipitation from solution.

The positions on the aromatic rings in the following discussions were numbered counterclockwise starting with the hydroxyl or methoxyl para to the methyl group:



OXIDATION OF 4-METHYLPYROCATECHOL

PRODUCT IDENTIFICATION

The peroxyacetic acid oxidations of pyrocatechol and 4-methylpyrocatechol have been found to give good yields of muconic acid derivatives, especially with the use of metal catalysts (23, 25, 47). However, only the material that could be precipitated from solution was investigated in these studies.

The oxidation of 4-methylpyrocatechol (4-MC) proceeded at a rate faster than any of the other substrates studied in this thesis; it was complete in one hour. This was also the simplest oxidation in that the fewest number of products were found, and they were all carboxylic acids. No neutral products were found in any significant amounts, although many very small peaks were detected by gas-liquid chromatography (GLC).

Carboxylic Acid Products

cis, trans-β-Methylmuconic acid (VI) was the first compound isolated from the 4-methylpyrocatechol oxidation: it precipitated from solution during and after the oxidation. The melting point of the crude white precipitate was

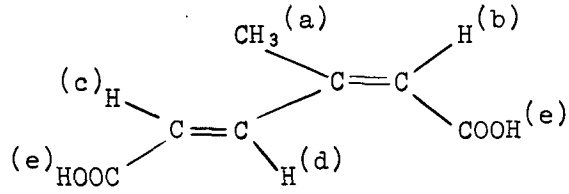
179.0-182.0° [lit. m.p. 178.0-179.0 (23)]. β-Methylmuconic acid (VI) was isolated by Elvidge, Linstead, and Sims (25) from similar reaction conditions. This product was then examined by infrared and NMR, giving the results shown in Table I.

TABLE I

SPECTRAL DATA FOR β-METHYLMUCONIC ACID (β-MMA)

Infrared[a]		NMR (D_6-DMSO)			
cm.$^{-1}$	Assignment	δ, p.p.m.	Multiplicity	J, Hz	Number of Protons
2680 (M)	Carboxyl	2.04 (a)	2	1.5	3
2590 (M)	-OH	∿6.00 (b)	∿5	1	1
1688 (VS)	C=O	6.18 (c)	4	16,1	1
1628 (MS)	C=C	8.48 (d)	4	16,1	1
1600 (M)		12.8-11.7 (e)	very weak — probably hydroxyl protons		

[a]Solid in KBr pellet.



VI

The NMR results agree with the assigned structure and confirm the trans-configuration of the vinyl hydrogens due to the large coupling constant. Therefore, the spectral data support the structure previously assigned (25) to the acid of m.p. 179° as cis, trans-β-methylmuconic acid (β-MMA).

Although β-MMA was often isolated as a precipitated solid, it was also possible to isolate it from product mixtures by gas-liquid chromatographic separation of the TMS derivative. Its identity was then confirmed by comparison of GLC retention times (TMS derivative) and infrared spectra (free acid) with those of an authentic specimen.

The remaining products from the 4-methylpyrocatechol oxidation were collected as methyl esters and identified as such. All of the carboxylic acid products found are listed in Table II with the retention times of the corresponding methyl and trimethylsilyl esters.

TABLE II

RETENTION TIME OF CARBOXYLIC ACID PRODUCTS

Product[e]	Retention Time, min.	
	Methyl Ester[a]	TMS Ester[b]
γ-Methyl-lactone (VIII)	7.7	7.5
γ-Hydroxy-β-methyl-lactone (IX)	11.3	--
β-Methyl-lactone (VII)	21.0	12.8
U2 (lactone)	--	14.2
U2A[c]	--	15.3
β-Methylmuconic acid	26.3[d]	18.4
U3 (lactone)	28.4[d]	21.6
U4 (lactone)	31.0[d]	23.5

[a] Carbowax 20M, 180°, 120 ml./min. He flow rate.
[b] SE-30, 165°, 120 ml./min. He flow rate.
[c] Not found in 4-methylpyrocatechol product but in a few later products.
[d] These methyl esters appeared in product chromatograms but were not collected and identified; they generally correspond to the indicated TMS ester.
[e] Complete names and structures of these products are given later.

A major product found from this and all other oxidations was γ-carboxymethyl-β-methyl-$\Delta^{\alpha,\beta}$-butyrolactone (VII), which will be referred to in the future as β-methyl-lactone (β-ML). This product has also been identified by Elvidge and coworkers (25). The methyl ester (VIIe) which was initially examined by infrared and NMR contained a small amount of impurity (< 2%). Therefore,

the ester was recollected from the gas chromatograph in order to give a pure sample for mass spectrum analysis.

β-Methyl-lactone was also prepared by an unambiguous route through the action of sulfuric acid on 2-nitro-p-cresol (48). This known material was methylated, and its infrared and NMR spectra were found to match those of the suspected product. For comparison to future related products, these spectral data are presented in Tables III and IV.

TABLE III

SPECTRAL DATA FOR β-METHYL-LACTONE (β-ML) AND METHYL ESTER

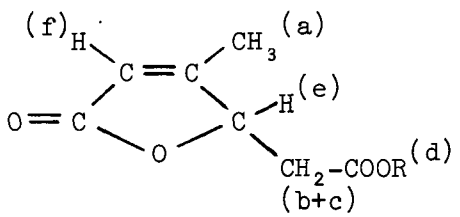
Free Acid (VII)

Infrared[a]		NMR (D_2O)				
cm.$^{-1}$	Assignment	δ, p.p.m.	Multiplicity	J, Hz	Number of Protons	
3360 (MW)	O-H	2.04 (a)	4	0.8	3	
2580 (broad)	COOH H-bond	2.68 (b)	4	16.5,7.5	1	ABX
		3.13 (c)	4	16.5,4.5	1	ABX
1730 (VS)	C=O	5.43 (e)	16	4,0.8	1	ABX
1687 (VS)	C=O	6.00 (f)	5	1.5	1	
1640 (S)	C=C					

Methyl Ester (VIIe)

Infrared[b]		NMR ($CDCl_3$)				
1755 (VS)	C=O	2.10 (a)	3	1	3	
1740 (VS)	C=O	2.62 (b)	4	16,7.5	1	ABX
1642 (M)	C=C	2.85 (c)	4	16,4.5	1	ABX
		3.77 (d)	1	--	3	
		5.26 (e)	15	~6,1	1	ABX
		5.88 (f)	~5	1.5	1	

[a] Solid in KBr pellet.
[b] Liquid between NaCl plates.



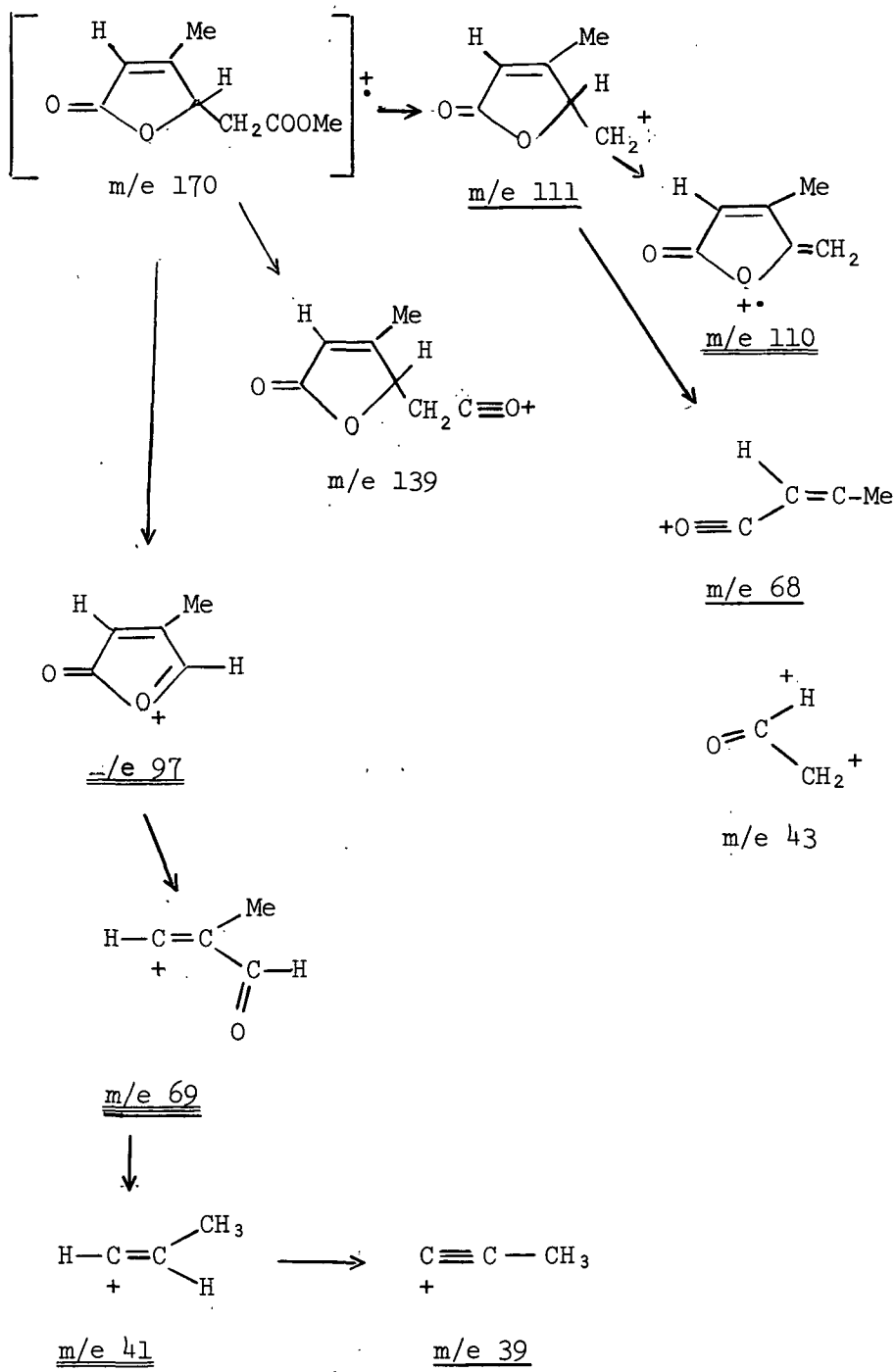
VII: R = H

VIIe: R = CH_3

TABLE IV

MASS SPECTRAL DATA FOR β-METHYL-LACTONE (β-ML) METHYL ESTER AND INTERPRETATION

m/e	% of Base	
172	0.4	(P+2)
171	2	(P+1)
170	20	(P)
142	6	
139	14	
138	9	
112	3	
111	30	
110	78	
98	7	
97	93	
96	27	
83	3	
82	9	
71	3	
70	6	
69	100	(Base)
68	38	
67	9	
59	11	
57	3	
55	6	
54	3	
53	6	
51	3	
45	3	
44	7	
43	22	
42	15	
41	70	
40	27	
39	42	
38	6	
32	4	
31	7	
29	13	
28	22	
27	10	
18	12	
15	26	



One interesting point in the NMR spectrum is the nonidentical methylene protons (b and c) which give rise to an ABX coupling where the X-group is the (e) hydrogen. The correct chemical shifts in the AB portion for protons (b) and (c) were calculated as described by Bible (49) and Garbisch (50).

The mass spectrum also gave fairly predictable results; fragmentation occurred along known routes for lactones, branched compounds, and carboxylate esters (51). The intensities noted for the peaks were determined by measuring the height of the peaks. The parent peak at 170 is evident, and the fragments that give rise to the higher mass numbers evidently come from the side chain (CH_2COOCH_3) breaking at different points. The base peak at m/e 69 apparently results from the loss of carbon monoxide from the lactone in m/e 97.

The presence of the trimethylsilyl ester of β-methyl-lactone in the product mixture during quantitative analysis was confirmed by retention time comparison to the known ester and by collecting the "peak" and determining its infrared spectrum.

A second unknown product was identified as γ-carboxymethyl-γ-methyl-$\Delta^{\alpha,\beta}$-butyrolactone (VIII). This will simply be referred to as γ-methyl-lactone (γ-ML). The methyl ester of this lactone (VIIIe) was collected (GLC) and found to contain less than 1% impurity as determined by GLC. Infrared, NMR, and mass spectral analyses were run on this compound, giving the results shown in Tables V and VI.

The parent peak of this compound in the mass spectrum is apparently at m/e 170. The intensity of this peak relative to lower mass peaks increased with lower voltage confirming that it is indeed the molecular ion. The following fragmentation pattern agrees well with what would be predicted based on the known β-methyl-lactone ester. Both the infrared and NMR spectra support the proposed structure. The hydrogen (e)

TABLE V

SPECTRAL DATA FOR γ-METHYL-LACTONE (γ-ML) AND METHYL ESTER

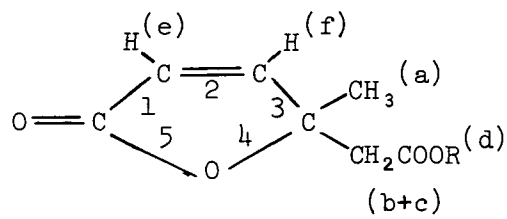
Methyl Ester (VIIIe) Infrared,[a] cm.$^{-1}$	Assignment	Free Acid (VIII) Infrared,[b] cm.$^{-1}$
--		∿3500 (M)
3080 (W)	=C-H	3100 (M)
2980 (MW)	CH_3	2990 (MW)
2930 (MW)	CH_2	2930 (M)
1755 (VS)	C=O	1775 (VS)
--	C=O	1740 (VS)
1640 (W)	C=C	1640 (W)
1610 (W)	C=C	1600 (W)
1440 (M)		1450 (M)
--		1400 (MS)
1360 (M)		1300 (MS)
1228 (M)		1200 (MS)
1168 (M)		1170 (M)
1122 (M)		1124 (M)
1105 (MS)		1105 (MS)
1057 (M)		1040 (MS)
956 (M)		955 (M)
820 (M)		820 (M)

Methyl Ester (VIIIe)

NMR ($CDCl_3$)

δ, p.p.m.	Multiplicity	J, Hz	Number of Protons	
1.57 (a)	1	--	3	
2.69 (b)	2	15	1	AB
2.91 (c)	2	15	1	AB
3.68 (d)	1	--	3	
6.03 (e)	2	6	1	
7.65 (f)	2	6	1	

[a] Liquid on KBr micropellet.
[b] Solid in KBr pellet.



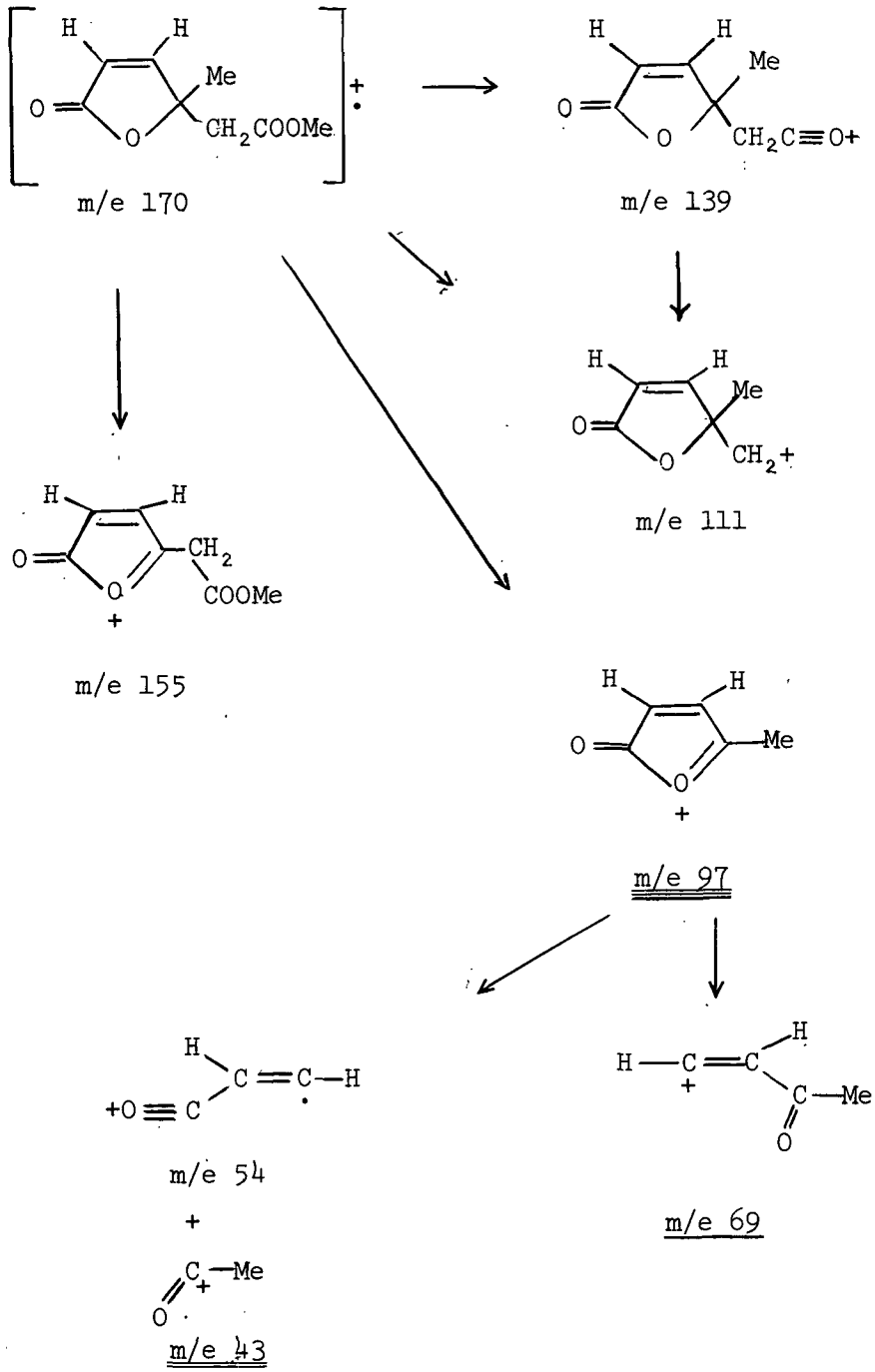
VIII: R = H

VIIIe: R = CH_3

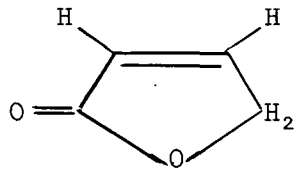
TABLE VI

MASS SPECTRUM FOR γ-METHYL-LACTONE (γ-ML)
METHYL ESTER AND INTERPRETATION

m/e	% of Base	
172	0.1	(P+2)
171	0.7	(P+1)
170	4	(P)
155	4	
139	4	
138	2	
127	6	
117	2	
113	20	
111	5	
110	6	
99	3	
98	9	
97	100	(Base)
95	2	
85	5	
83	3	
82	2	
79	3	
74	2	
69	32	
68	5	
59	14	
55	5	
54	7	
53	4	
51	2	
43	49	
42	8	
41	10	
40	4	
39	12	
29	5	
28	6	
27	6	
26	5	
18	6	
15	21	



has almost exactly the same δ-value as the corresponding one on β-methyl-lactone. The δ values for (e) and (f) agree with those of known $\Delta^{\alpha,\beta}$-butyrolactone (52):



The δ values and splitting found for the methyl group (a) and methylene protons (b+c) in β-methyl-lactone are consistent with their being bonded to the same γ-carbon on the lactone ring.

The mass spectrum agrees with the expected fragmentation of γ-methyl-lactone methyl ester giving a base peak resulting from loss of the carboxylate side chain. However, the molecular ion can also lose a methyl group at the branch point to give the m/e 155 peak. The m/e 43 peak has been found by Friedman and Long (53) to be common for γ-methyl unsaturated butyrolactones. This evidently results from the common cleavage of the 3 and 5 bonds to give $O{=}\overset{+}{C}{-}CH_3$ as indicated in Table VI. The remaining fragments can be formed in much the same way as from the β-methyl-lactone methyl ester.

Therefore, the spectral evidence strongly supports the γ-methyl-lactone structure which has not been reported in the literature. The assigned structure is also consistent with formation of the compound from 4-methylpyrocatechol. There appears to be no other structure that will fit the spectral data.

The identity of the γ-methyl-lactone peak in the chromatogram of the trimethylsilyl ester products was determined in two ways. First, the free acid was obtained and silylated. GLC analysis of this TMS ester gave a peak having the same retention time as one of the peaks in the silylated product mixture. The free acid was prepared by a microhydrolysis of the available γ-methyl-lactone methyl ester:

the ester (10 mg.) was heated in 1 ml. of 10% hydrochloric acid on a steam bath for several hours. After standing at room temperature for one day, the entire product was concentrated to dryness, giving the free acid.

As further evidence that this was the γ-methyl-lactone-TMS ester, the silylated product having that retention time was collected (it subsequently hydrolyzed to the free acid in the air), and a microinfrared analysis was carried out. This spectrum is also shown in Table V alongside that of the known methyl ester. The two spectra would not be expected to be identical, but there is enough agreement to show that this is indeed the γ-methyl-lactone.

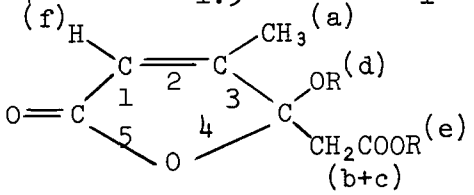
The fourth product found from the 4-methylpyrocatechol oxidation was identified as γ-carboxylmethyl-γ-hydroxy-β-methyl-$\Delta^{\alpha,\beta}$-butyrolactone (IX), hereafter to be referred to as γ-hydroxy-lactone (γ-HL). The dimethyl ester of this lactone (IXe) was collected (GLC), and the resulting spectral analyses are shown in Tables VII and VIII. The sample used for the spectral analyses was found by GLC to contain about two percent impurity.

TABLE VII

SPECTRAL DATA FOR DIMETHYL ESTER OF γ-HYDROXY-β-METHYL-LACTONE

Infrared[a]		NMR ($CDCl_3$)			
$cm.^{-1}$	Assignment	δ, p.p.m.	Multiplicity	J, Hz	Number of Protons
3080 (W)	C=C-H	2.04 (a)	2	1.5	3
1770 (S)	C=O	2.88 (b)	2	15	1 } AB
1740 (S)	C=O	3.08 (c)	2	15	1 } AB
1700 (MW)	C=O	3.17 (d)	1	--	3
1660 (MW)	C=C	3.63 (e)	1	--	3
		5.97 (f)	4	1.5	1

[a] Liquid on KBr micropellet.

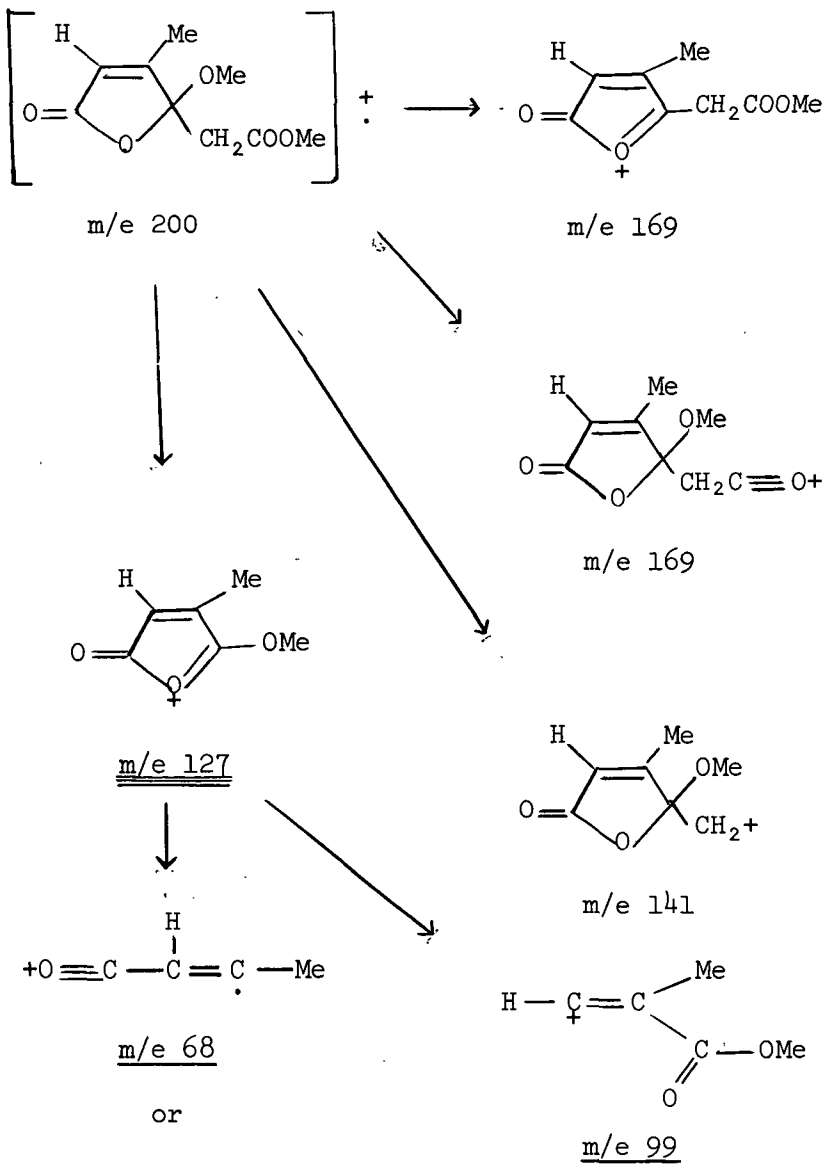


IX: R═H
IXe: R═CH_3

TABLE VIII

MASS SPECTRAL DATA FOR γ-HYDROXY-LACTONE DIMETHYL ESTER AND INTERPRETATION

m/e	% of Base
202	0.2 (P+2)
201	1.1 (P+1)
200	1.6 (P)
171	1
170	6
169	15
168	3
155	2
141	5
137	.3
133	3
129	1
128	8
127	100 (Base)
126	2
125	4
113	2
111	2
110	4
109	2
101	8
100	2
99	31
97	5
96	3
82	4
81	3
69	10
68	28
67	9
59	34
57	4
55	5
53	6
45	3
44	3
43	11
42	8
41	8
40	22
39	22
38	2
31	2
29	13
28	8
27	6
18	5
15	7

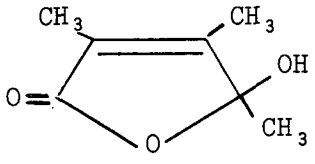


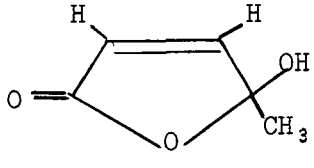
The mass spectrum shows a very weak m/e 200 peak. However, a lower voltage spectrum gave a larger m/e 200 peak relative to the fragments at m/e 170 and 169. Therefore, m/e 200 is the molecular ion.

The infrared spectrum shows the presence of unsaturation and carbonyl groups. The NMR, however, pins down the structure by showing the same methyl (a), methylene (b+c), methyl ester (e), and olefinic hydrogen (f) as for the β-methyl-lactone ester, with only slight shifts. The only difference in the two NMR spectra is the replacement of the methine hydrogen by the methoxyl group (d). Here again, the chemical shifts and splittings are consistent with this structure.

The mass spectrum further supports this conclusion. The base peak again arises from loss of the carboxylate side chain at the γ-carbon, leaving the lactone residue at m/e 127. Either of the two methoxyls can be lost to give a m/e 169 fragment. Cleavage at the 3 and 5 bonds in the lactone ring must occur to give the m/e 68 fragment.

Hence, all of the spectral results support the structure of the γ-hydroxy-lactone. However, there was some initial doubt as to the stability of a compound that possesses a hemiacetal-like carbon. A literature search revealed two studies of γ-hydroxy-$\Delta^{\alpha,\beta}$-butyrolactones having the following structures (54, 55).





Both compounds are very similar to the hydroxyl-lactone product (IX) and were found to be stable in both dilute acidic and alkaline solutions.

It was discovered that the γ-hydroxy-lactone free acid (IX) decarboxylated when injected on the gas chromatograph. An oxidation product solution was

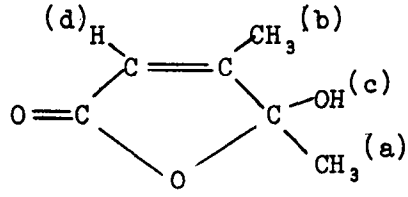
concentrated in vacuo, dissolved in ether and chromatographed (GLC). A resulting large peak was collected and found by infrared and NMR analysis to be γ-hydroxy-β,γ-dimethyl-$\Delta^{\alpha,\beta}$-butyrolactone (X). There was no evidence that this was a direct reaction product. The spectral data are shown in Table IX. The infrared gave evidence for hydroxyl, carbonyl, and olefin groups. The NMR gave further evidence for the hydroxyl group while indicating a methyl group on a double bond (b), an olefinic proton adjacent to a carbonyl group (d), and a methyl group adjacent to an oxygen. Both the splitting and chemical shifts of (b) and (d) are almost the same as the corresponding groups in γ-hydroxy-lactone (IX).

TABLE IX

SPECTRAL DATA FOR γ-HYDROXY-β,γ-DIMETHYL-$\Delta^{\alpha,\beta}$-BUTYROLACTONE

Infrared[a]		NMR ($CDCl_3$)			
$cm.^{-1}$	Assignment	δ, p.p.m.	Multiplicity	J, Hz	Number of Protons
3270 (S)	-OH	1.64 (a)	1	--	3
3080 (W)	C=C-H	2.08 (b)	2	1.5	3
1735 (VS)	C=O	~4.08 (c)[b]	broad	--	1
1657 (M)	C=C	5.74 (d)	4 or 5	1.5	1

[a] Liquid on KBr micropellet.
[b] Peak disappeared when D_2O was added.



X

The attempted quantitative analysis of γ-hydroxy-lactone, however, was unsuccessful with the TMS derivatives. When the trimethylsilyl derivatives were prepared, there was no evidence of a peak for γ-hydroxy-lactone (IX). All of the significant peaks had been accounted for. Therefore, a microhydrolysis was run on the dimethyl γ-hydroxy-lactone ester (IXe) as was done with γ-methyl-lactone (VIIIe). However, silylation of this microhydrolysis product mixture gave only several small peaks; none of these corresponded to any peaks found from the silylated oxidation products. Thus, decomposition of the γ-hydroxy-lactone must have taken place at some time during the silylation procedure and analysis.

The solvent used, dimethylformamide, should not have caused any problems, since it has been used as a solvent for chromatography of a large number of carboxylic acids (56). It is also commonly used in silylations (57).

Therefore, there would seem to be only two probable explanations remaining. One possibility is that the reaction between bis(trimethylsilyl)trifluoroacetamide, the silylating agent, and γ-hydroxy-lactone does not lead simply to the TMS ester but gives some other product. A second reason might be decomposition in the gas chromatograph. Although the methyl ester of the hydroxy lactone is stable under the analysis conditions, the TMS ester may not be. The TMS group could be lost giving the free acid which can then decarboxylate as has been shown.

However, an approximate figure for the yield of γ-hydroxy-lactone was calculated. In Table LXXV in Appendix VI, calculations were made from gas chromatograms

of the product methyl esters. From the peak areas obtained, the relative amount of γ-hydroxy-lactone present based on the γ-methyl-lactone was calculated. This fraction (0.14 for 4-MC oxidation) was multiplied by the percentage of γ-methyl-lactone found in Table XI to give an approximate figure for the γ-hydroxy-lactone yield. This result is approximate because the degree of methylation of the various products was unknown.

Only one other product was consistently found in significant amounts from the 4-methylcatechol oxidation. This compound was denoted U2 because it was not definitely identified. The spectral data are shown in Table X. This product was found only in the silylated product mixtures. Unfortunately, the spectrum was weak, and impurities were present making it impossible to arrive at a definite conclusion for a structure. The structure drawn in Table X only roughly fits the NMR data and should not be thought of as the definite structure but only as a possibility. The protons at δ 6.15 and 7.68 are in almost the exact same position as the two vinyl protons in γ-methyl-lactone. Although this is proposed to be a δ-lactone, examination of other NMR spectra indicates that the chemical shifts of the vinyl hydrogens on a carbon-carbon double bond α,β to a carboxyl group would be about the same in a γ- or δ-lactone (58).

The chemical shift of δ 1.43 and single peak indicate that this methyl group is linked to a carbon adjacent to an oxygen atom. Probable methylene hydrogens at δ ∿ 2.08 appear to be coupled with the vinyl hydrogen (d) although the coupling constant is somewhat smaller than would normally be expected.

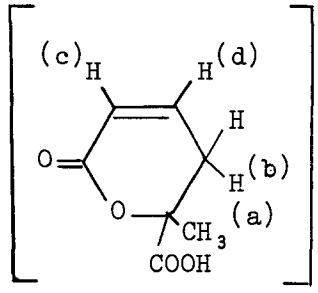
Two other products at longer retention times (overlapping) were consistently present in small amounts in the silylated product. These were noted as U3 and U4. Infrared analyses (Appendix III) indicated only that they are probably unsaturated lactone structures.

TABLE X

SPECTRAL DATA FOR U2

Infrared[a]		NMR (DMSO)			
cm.$^{-1}$	Assignment	δ, p.p.m.	Multiplicity	J, Hz	Number of Protons
3350 (MS)	-OH	1.43 (a)	1	--	3
3100 (MS)	=C-H	∿2.08 (b)	4	11,2	2 (AB?)
2600 (MW) }	Carboxyl -OH	6.15 (c)	2	6	1
2500 (MW) }		7.68 (d)	4	6,2	1
1730 (VS)	C=O				
1700 (VS hump)	C=O	Probable Impurities			
1640 (VW)	C=C	1.50	1	--	< 1
1613 (W)	C=C	3.83	broad	--	> 100
1000 (MS)		4.12	2	1	∿ 1
924 (MS)					

[a]Solid in KBr micropellet.



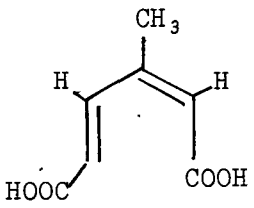
?

XI

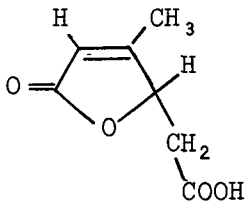
One other product was found in the silylated oxidation product of other substrates. It was not found in the 4-methylpyrocatechol oxidation product but will be noted here to complete the discussion of the carboxylic acid products found. This unknown was denoted U2A and was not collected or analyzed.

PRODUCT YIELDS

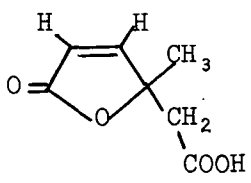
A summary of all of the products found from the peroxyacetic acid oxidation of 4-methylpyrocatechol would be as follows:



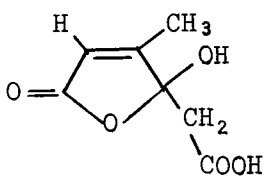
VI



VII



VIII



IX

+ unknowns: U2, U3, U4

This constitutes a complete analysis of most of the products detected by gas chromatography. The only major product that was not conclusively identified was U2. The other unidentified products were present in much smaller amounts (< 5%). The percentage yields as determined by product silylation are reported in Table XI. All reactions went to completion. The hydrogen peroxide content is the amount present at the beginning of the reaction. This concentration generally dropped slightly by the end of all oxidations.

TABLE XI

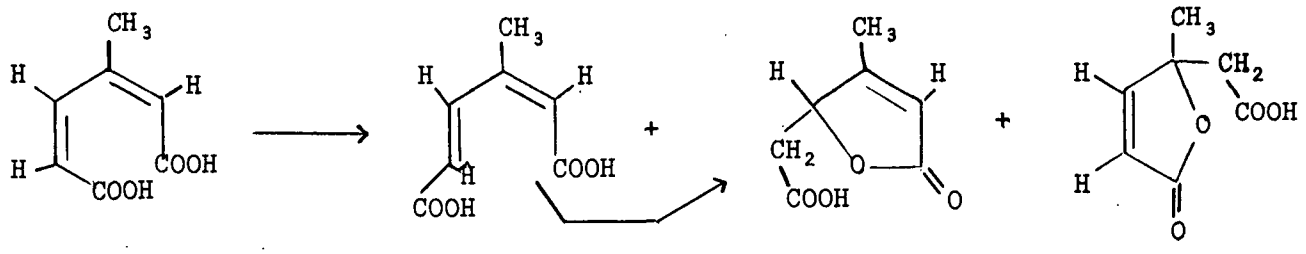
PRODUCT YIELDS FROM 4-METHYLPYROCATECHOL OXIDATION

Reaction No.	Reaction Time, hr.	Product Yield, % of theoretical: Muconic Acids	Hydroxy-lactone[a]	Total	H_2O_2, %
2675-25-5	1.5	54.4	5.0	59.4	0.34
2617-97[b,c]	4	63.9	4.6	68.5	0.3
2675-87-5	22	48.5	4.7	53.2	0.30
2617-109[b,c]	36	53.8	6.6	60.4	0.5
2617-141[b,c]	40	65.7	5.0	70.7	1.0
2668-87[d]	25	52.2	4.0	56.2	1.4
Averages		56.4	5.0	61.4	

Reaction No.	Muconic Acids, % of theoretical: γ-ML (VIII)	β-ML (VII)	U2	β-MMA (VI)	U3+U4
2675-25-5	4.4	35.5	9.6	2.0	2.9
2617-97[b,c]	4.1	32.9	11.0	12.3	3.6
2675-87-5	5.4	33.7	5.0	2.4	2.0
2617-109[b,c]	2.3	46.9	2.0	0.7	1.9
2617-141[b,c]	5.1	36.0	15.6	2.5	6.5
2668-87[d]	4.9	28.8	10.5	2.6	5.4

[a] Hydroxy-lactone figure approximated from other data.
[b] Remaining peroxyacid not reduced.
[c] Entire product solution concentrated, not worked up.
[d] Entire product solution freeze dried.

The three products, γ-methyl-lactone (VIII), β-methyl-lactone (VII), and cis, trans-β-methylmuconic acid (VI), are all closely related, being isomers of cis, cis-β-methylmuconic acid (XII):



XII VI VII VIII

The conversion of cis, trans-β-methylmuconic acid has been shown by Elvidge and co-workers (25) to give β-methyl-lactone under very mild conditions. However, a cis configuration at the vinyl double bond would be required to form the γ-methyl-lactone. Also, it will be shown later that U2, U3, and U4 are all related to cis, trans-β-methylmuconic acid and the two lactones. Therefore, in future discussions, these six products will often be collectively referred to as "muconic acids."

It was found that about 15% of the β-methyl-lactone was lost when a known amount was run through the work-up procedure. Therefore, results for 2675-25-5 and -87-5 would be somewhat greater had they been simply concentrated and analyzed as were the other runs shown. The product that was freeze dried gave essentially the same result as the other methods of product preparation. Since freeze drying should not have any effect on the products, this indicates that the other work-up methods were also satisfactory.

But even more important was the loss of product during the reaction. β-Methyl-lactone (0.6 g.) and β-methylmuconic (0.1 g.) acid were individually dissolved in 5% peroxyacetic acid solutions and stored for 24 hours. Subsequent work-up of the lactone reaction solution gave 79% yield of β-methyl-lactone which was about that found from

just the work-up control (85%). However, when the β-methylmuconic acid control was worked up and analyzed, a 47% yield of β-methyl-lactone was found: no muconic acid was detected. [β-Methylmuconic acid has been shown to form β-methyl-lactone under mildly acidic conditions (25).] Other work showed that neither of these products consumed any peroxyacetic acid. Therefore, β-methylmuconic acid, in the acidic reaction solution, must form some other compound besides β-methyl-lactone that is not detectable by the GLC analysis methods used.

STOICHIOMETRY

The results of the stoichiometry determinations carried out on the 4-methylpyrocatechol oxidations are shown in Table XII. (See Appendix VI for sample calculation.) The titration procedure used to determine the stoichiometry (moles oxidant to moles substrate) was found to be very reproducible and was not affected by the presence of β-methyl-lactone. Consequently, it would seem that none of the other known carboxylic acid products would interfere in the iodimetric titration either. The "% Reaction" figure is the percentage of substrate (4-MC) consumed.

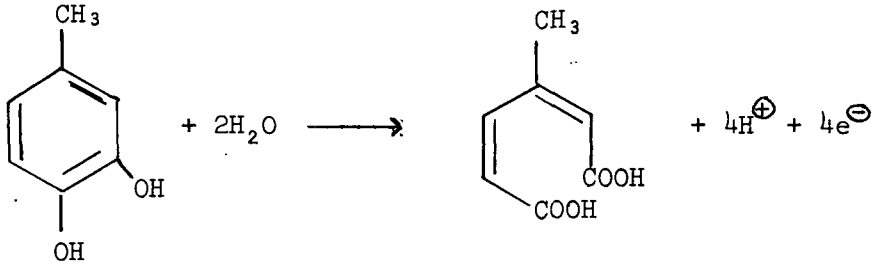
TABLE XII

4-METHYLPYROCATECHOL STOICHIOMETRY

Reaction No.	Reaction Time, hr.	% Reaction	Stoichiometry	H_2O_2, %
2601-31-1	30	100	2.07	0.63
31-2	30	100	2.08	0.63
2675-13-5	22.5	100	2.20	0.09
2601-43-1	16	100	2.12	0.86
43-2	16	100	2.12	0.86
49-1	0.5	89.4	1.89	0.9
49-2	0.5	92.8	1.89	0.9

These results indicate that about 2.1 moles of peroxyacetic acid is required to oxidize one mole of 4-methylpyrocatechol. This agrees very well with the products found. The reduction of peroxyacetic acid to acetic acid is a two-electron step while the conversion of 4-methylpyrocatechol to muconic acids is a four-electron oxidation:

$$CH_3CO_3H + 2H^{\oplus} + 2e^{\ominus} \longrightarrow CH_3CO_2H + H_2O$$



Therefore, a theoretical stoichiometry of 2.0 would be predicted if muconic acids were the only products. However, oxidation to γ-hydroxy-lactone would require three moles of peroxyacid and would, therefore, give an overall reaction stoichiometry greater than 2.0, depending on the amount present. Since Table XI shows that the γ-hydroxy-lactone amounts to about 8% of the products found, a stoichiometry of 2.08 would be predicted; this agrees surprisingly well with what was found. It is, therefore, apparent that the balance of the product that was not found resulted from the same amount of peroxyacid consumption per mole as did those products that were identified.

It can be seen from the last two tables that the concentration of hydrogen peroxide had little effect on the product yield and stoichiometry results. The lower stoichiometry results (1.89) could have come from the difficulty of synchronizing the time of titration with the moment the product solution was reduced because of the fast reaction.

It would have been desirable to run a control oxidation containing hydrogen peroxide and no peroxyacetic acid. However, if the reaction was to be similar to the peroxyacetic acid oxidation, the hydrogen peroxide would have to be run in a solvent that consisted of about 80% acetic acid and 20% water. When hydrogen peroxide was simply mixed with a solvent such as this, an appreciable amount of peroxyacetic acid was generated as shown in Table XIII:

TABLE XIII

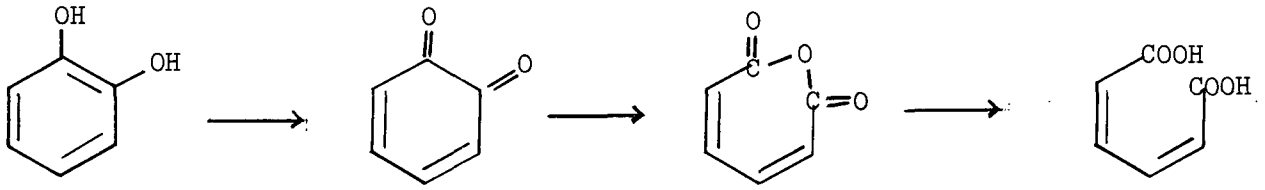
FORMATION OF PEROXYACETIC ACID FROM HYDROGEN PEROXIDE AND ACETIC ACID

Time, hr.	H_2O_2, %	AcO_2H, %
0	4.55	0
7	4.30	0.51
19	3.89	1.34
32	3.56	2.05
55-1/2	3.00	3.22
72	2.62	3.93

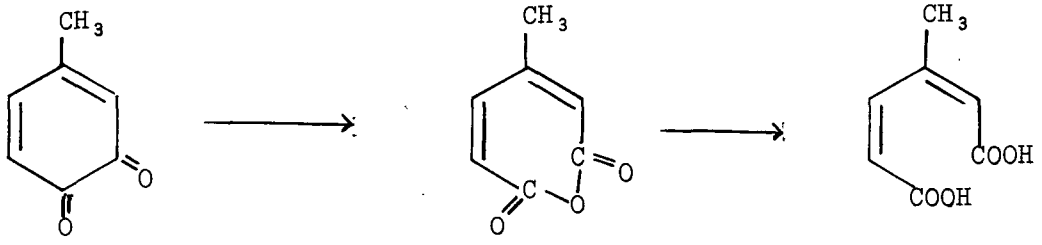
Since peroxyacetic acid is generally more reactive under acidic conditions than hydrogen peroxide, a small amount could probably cause as much oxidation as the hydrogen peroxide. It can also be seen that any reactions run for a long time would have an appreciable amount of peroxyacid present. Thus, the effect of hydrogen peroxide alone could not be studied in the solvent system used.

OXIDATION MECHANISM

The currently proposed theory for the general mechanism of peroxyacid oxidation resulted from studies by Wacek and Fiedler (23), and Karrer, et al. (59). They proposed an o-benzoquinone intermediate in the oxidation of catechol to muconic acid followed by oxidation to muconic acid anhydride which would finally hydrolyze



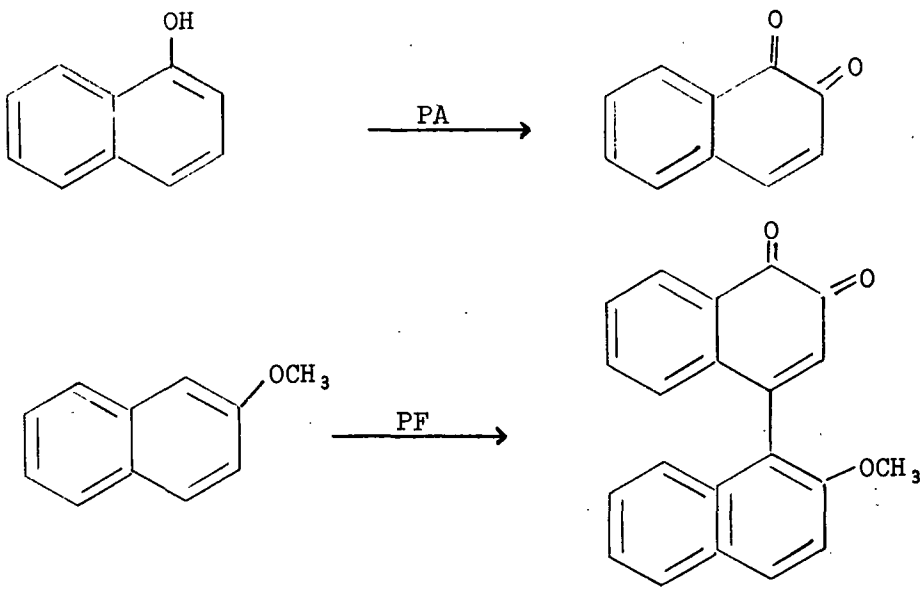
to muconic acid. Karrer and coworkers and more recently Elvidge, et al. (19) actually isolated the anhydride formed by the oxidation of 4-methyl-o-benzoquinone (XIII) by monoperoxyphthalic acid in chloroform and ether, respectively. The anhydride was



XIII

found to be extremely sensitive to moisture, forming muconic acids. Similarly, 4-carboxy-o-benzoquinone (60) and o-benzoquinone (61) were oxidized by peroxyacetic acid to give muconic acids; the anhydride was not isolated.

Although neither the o-quinone nor the anhydride has been isolated from the peroxyacid oxidation of any simple aromatic phenol, o-quinones have been found from the peroxyacetic acid (PA) oxidation of α-naphthol (62) and the peroxyformic acid (PF) oxidation of β-naphthol methyl ether (63) as indicated on the following page:



Therefore, there is good evidence for o-quinone intermediates. However, it was felt that stronger evidence for or against an o-quinone intermediate could be obtained by independently determining the complete product composition resulting from oxidation of the o-quinone.

Freshly prepared 4-methyl-o-benzoquinone was oxidized by peroxyacetic acid and subsequent work-up gave the results indicated in Table XIV. This reaction was essentially instantaneous. As a result of this fact, it was possible to crudely determine the stoichiometry. An equimolar solution of 10% peroxyacetic acid and 4-methyl-o-benzoquinone was prepared. After a few minutes when the solution had cooled, more peroxyacetic acid was added, but no further apparent heating took place. This is good evidence of a stoichiometry of 1.0 which would be theoretically required to produce one mole of muconic acid from the o-quinone.

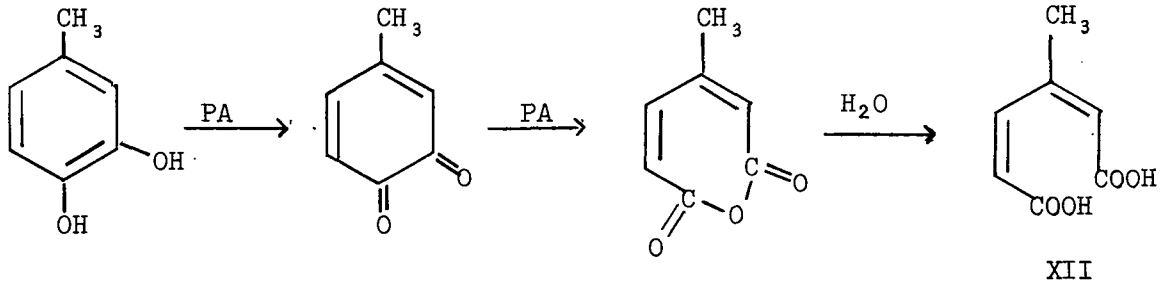
The results in Table XIV show that a significantly higher total yield of products was obtained after only five minutes reaction as compared to 26 hours reaction. Conversely, a larger number of products were formed with longer reaction time. GLC of the methylated o-quinone oxidation

TABLE XIV

PRODUCT YIELDS FROM 4-METHYL-o-BENZOQUINONE OXIDATIONS

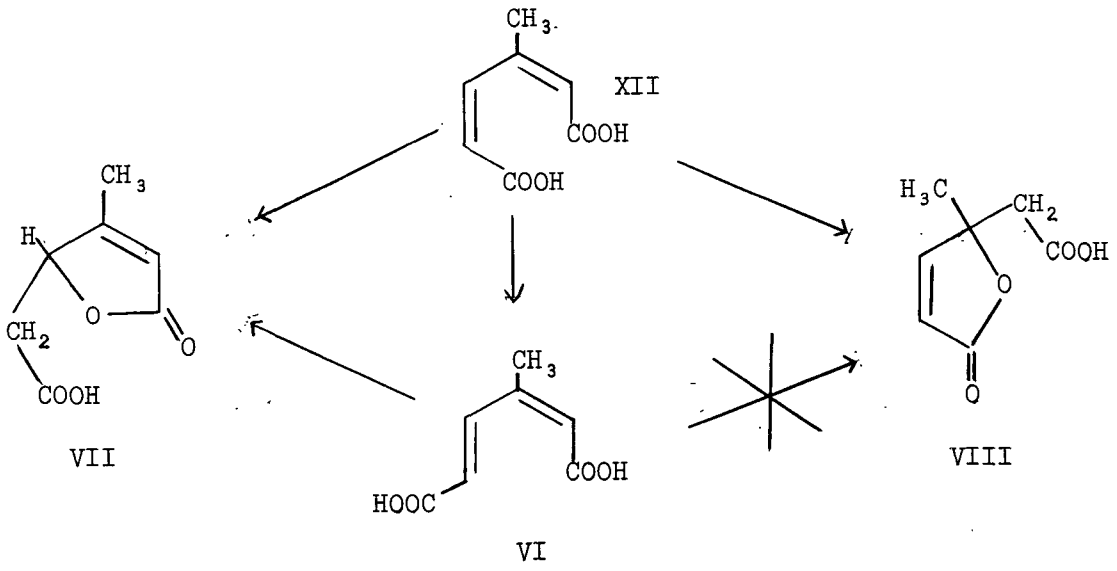
Reaction No.	Reaction Time, hr.	Yield, % of theoretical					
		γ-ML (VIII)	β-ML (VII)	U2	β-MMA (VI)	U3+U4	Total
2675-158	0.1	7.7	44.1	--	18.6	--	70.4
2675-155-4	26	4.4	32.6	11.4	3.7	3.3	55.4

product showed that no γ-hydroxy-lactone was formed (Table LXXV). This, however, was the only difference between the o-quinone and catechol oxidation products. Neither oxidation gave any volatile products and the gas chromatogram of the silylated carboxylic products from the o-quinone (2675-155-4) was identical in every detail to that of the corresponding catechol product. Muconic acid yields were also the same. This product analysis, therefore, provides convincing evidence that the o-quinone is the intermediate in the peroxyacetic acid oxidation to muconic acids. Thus, the following reaction sequence can be written with a high degree of confidence:



XII

It seems logical that cis, cis-β-methylmuconic acid (XII) is the original product. Evidence for this initial configuration is given by the γ-methyl-lactone (VIII) found which could only be formed from a cis configuration at the vinyl double bond. The cis, cis-acid (XII) also forms the cis, trans-acid (VI) which apparently is the more stable form. The β-methyl-lactone (VII) can apparently form from either of these diacids.



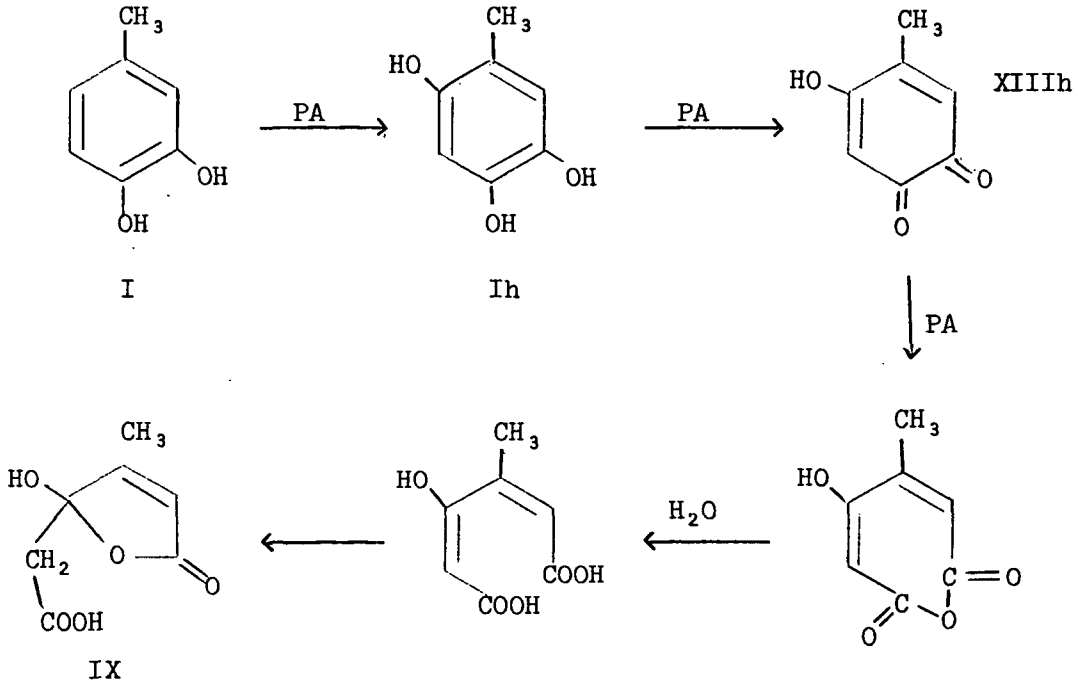
The unknowns U2, U3, and U4 were found only in the 4-methyl-o-benzoquinone product mixture that was stored for 26 hours. The accompanying drop of muconic acid yields with reaction time shows that these unknowns must be isomers of the three original products: β-methylmuconic acid and γ-methyl- and β-methyl-lactone. In addition, the overall drop in yield shows that other isomers must be formed that are not detectable by the gas chromatographic methods used.

The constant stoichiometry and product yields as a function of time for the 4-methylpyrocatechol oxidation show that the products do not react with the peroxy-acid. They also show that any isomerization of the initial products must occur during the first two hours.

The presence of the γ-hydroxy-lactone product has not been included in the previous discussion. Since it was not found from the 4-methyl-o-benzoquinone oxidation, it must result from oxidation of 4-methylpyrocatechol prior to o-quinone formation.

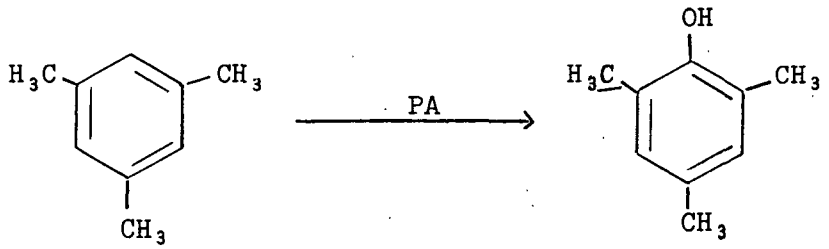
A simple initial hydroxylation step can be proposed to account for this product, giving 5-hydroxy-4-methylpyrocatechol (Ih) as the first intermediate. This could be

further oxidized at the ortho-hydroxyl groups to form the hydroxy-o-quinone (XIIIh) and finally yield γ-hydroxy-lactone (IX):



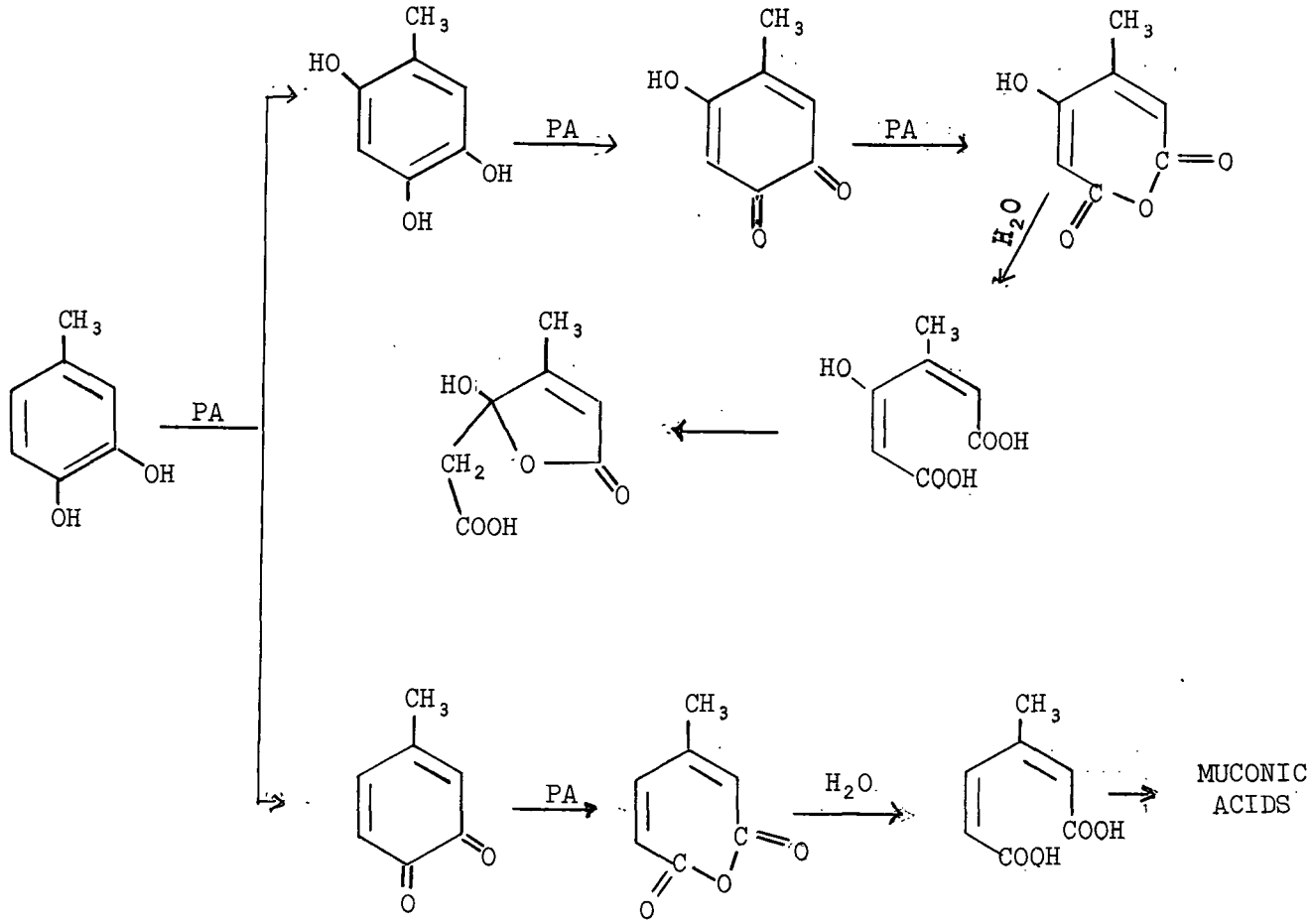
Simple hydroxylation has not generally been observed in aromatic systems because the hydroxylated product usually would be more reactive than the starting material. It, therefore, would be further oxidized so rapidly that little would ever be present in solution. However, in molecules where reactive sites are blocked by alkyl groups, simple hydroxylation has been observed (21, see p. 9).

Mesitylene was oxidized by peroxyacetic acid in this thesis under the same conditions that all other oxidations were run. One of the products formed was collected from the gas chromatograph and shown by subsequent infrared analysis to be hydroxymesitylene:



The infrared spectrum of this product was identical to that of known hydroxy-mesitylene. Mesitylene was chosen for analysis because the normal reactive positions, both ortho and para to the newly added hydroxyl, are blocked by methyl groups. It was thought that this would give the best chance of obtaining some hydroxylated starting material if any was formed. These results, therefore, clearly show that simple hydroxylation is definitely a possible reaction in the oxidation system employed in this study.

All of these studies, therefore, support the proposed reaction sequence noted earlier for the oxidation of 4-methyl-pyrocatechol to γ-hydroxy-lactone. As a result, the following overall reaction sequence can be proposed for the 4-methylpyrocatechol oxidation:



This shows that the initial attack of a peroxyacetic acid molecule can occur at either of two points on the ring: oxidation at the o-hydroxyls or, to a much lesser extent, hydroxylation at the C-5 position. After the hydroxylation step to give the trihydroxy compound, the two oxidation sequences are essentially identical.

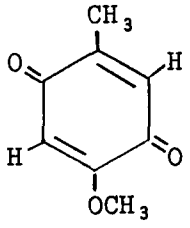
A 4-methylpyrocatechol oxidation was carried out in the presence of methylmethacrylate. Subsequent water dilution gave no polymer precipitate, indicating the absence of free radicals.

OXIDATION OF 4-METHYLVERATROLE

PRODUCTS

Neutral Products

The main product found from this reaction was 2-methoxy-5-methyl-p-benzoquinone (XIV). This was easily precipitated out of the product solution by dilution with water. The yellow material was filtered and its infrared spectrum



XIV

determined. The infrared was identical to Sadtler spectrum (prism) number 22030 (64) for 2-methoxy-5-methyl-p-benzoquinone. This product was volatile enough for quantitative analysis by gas chromatography (GLC).

One other neutral product (U1) was found from the 4-methylveratrole oxidation by GLC analysis but was not collected or identified. The yields of this product and the p-quinone are shown in Table XV.

Davidge and coworkers (28) studied this reaction under similar conditions and also found 2-methoxy-5-methyl-p-benzoquinone. However, they did not search for any other products.

Carboxylic Acid Products

All of the lactone products identified from the oxidation of 4-methylpyrocatechol were also present in the 4-methylveratrole (II) oxidation product mixture: β-methyl-lactone (VII), γ-methyl-lactone (VIII), and γ-hydroxy-lactone (IX). The methyl esters of these lactones were collected from the oxidation product, and their

TABLE XV

PRODUCT YIELDS FROM 4-METHYLVERATROLE OXIDATION[a]

Reaction No.	% Reaction	Product Yield, % of theoretical					H_2O_2, %
		U1	p-Quinone	Muconic Acids	Hydroxy[b] Lactone	Total	
2629- 90[c]	86.3	1.3	17.4	N.D.[d]	N.D.	N.D.	0.03
2675- 25-4	84.2	2.2	20.3	14.8	1.2	38.5	0.34
87-3	82.7	1.6	13.2	11.8	1.2	27.8	0.30
155-2[c]	81.5	1.7	18.2	N.D.	N.D.	N.D.	0.05
Averages		1.7	17.3	13.3	1.2	33.5	

Reaction No.	Muconic Acids, % of theoretical			
	γ-ML (VIII)	β-ML (VII)	U2	U3+U4
2629- 90[c]	N.D.	N.D.	N.D.	N.D.
2675- 25-4	1.0	6.5	6.2	1.1
87-3	1.0	6.4	3.3	1.1
155-2[c]	N.D.	N.D.	N.D.	N.D.

[a] All reactions were run about 30 hours.

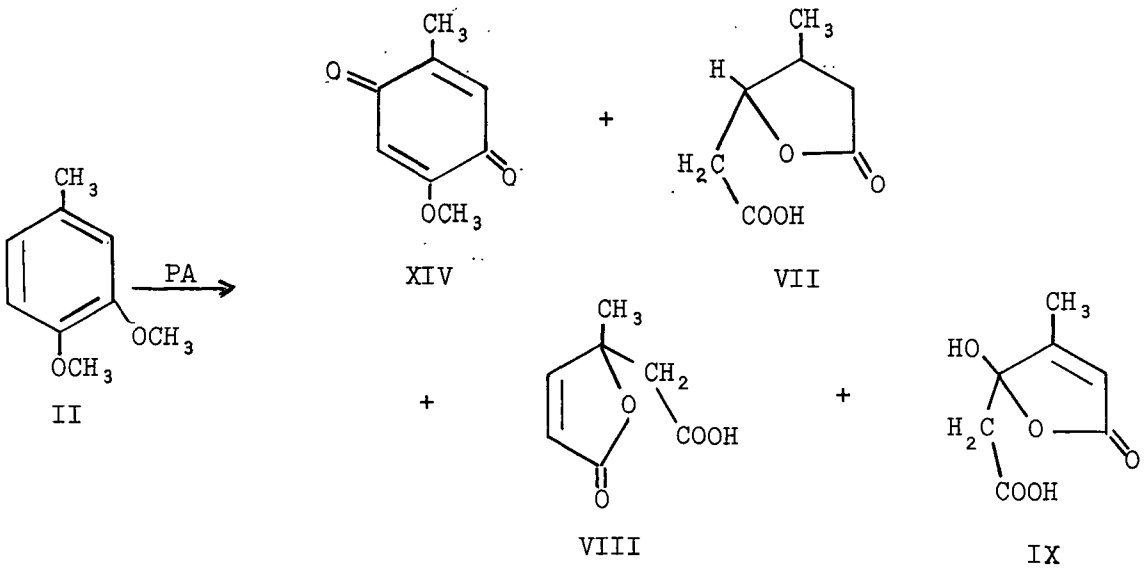
[b] Hydroxy-lactone yield approximated from other data.

[c] Alkaline extract was not worked up.

[d] N.D. = not determined.

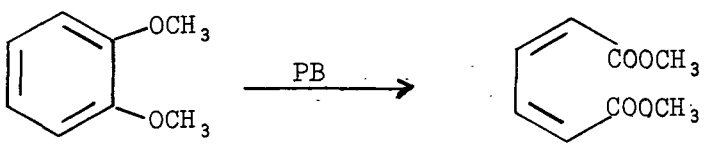
structures were confirmed by comparison of their infrared spectra with those of authentic compounds. The absence of β-methylmuconic acid in the silylated product mixture was probably due to the overall low yield of carboxylic acid products.

The products found from this reaction can be described as follows:

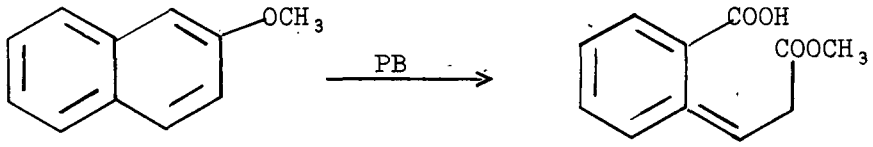


The yields of these products are shown in Table XV. The yield of γ-hydroxy-lactone was approximated from the factor determined in Table LXXV in Appendix VI.

Only a few studies have been reported in the literature on ring cleavage reactions of methoxybenzenes. 1,2-Dimethoxybenzene gave dimethylmuconate (1%) when



oxidized by peroxybenzoic acid in chloroform (27). Fernholz (30) found a monomethyl diacid (∿ 40%) when 2-methoxynaphthalene was oxidized by peroxybenzoic acid in benzene:



However, oxidation by aqueous peroxyacetic acid gave the free diacid (∿ 45%).

It would seem possible, therefore, that a muconic acid methyl ester could be a product of the 4-methylveratrole oxidation studied in this thesis. However, no methyl esters of any muconic acid products were found in the reaction mixtures. The methyl ester of β-methyl-lactone was found to be stable in the oxidation solution. Thus, any muconic acid ester formed should have been detected.

STOICHIOMETRY

The stoichiometry of the 4-methylveratrole oxidation was determined as reported in Table XVI. The 2-methoxy-5-methyl-p-benzoquinone product had no effect on the peroxyacid titration procedure used in the stoichiometry determinations, as was also found earlier for the muconic acids. The recovery of 4-methylveratrole from the oxidation product solution was found to be complete.

TABLE XVI

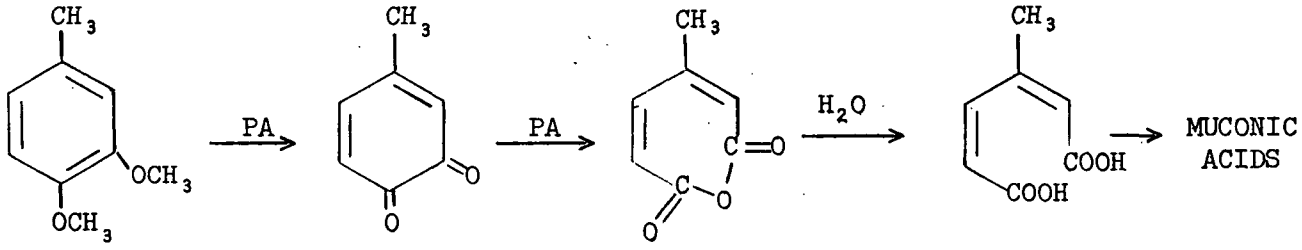
4-METHYLVERATROLE STOICHIOMETRY

Reaction No.	Reaction, %	Stoichiometry	H_2O_2, %
2601-157-1	17.8	2.20	1.2
144-1	38.7	2.64	0.8
144-2	59.4	2.66	0.8
144-3	71.1	2.81	0.8
144-4	80.5	2.90	0.8
2675- 13-2	81.6	2.92	0.09

The hydrogen peroxide content was higher than desired in most of these reactions. However, the results of the last determination (2675-13-2) containing very little hydrogen peroxide and an equivalent reaction (2601-144-4) containing about ten times as much peroxide were almost identical. This indicates that hydrogen peroxide had negligible effects. In support of this conclusion, Viel and coworkers (65) found that 1,2-dimethoxybenzene and 4-methylveratrole were not affected by hydrogen peroxide.

OXIDATION MECHANISM

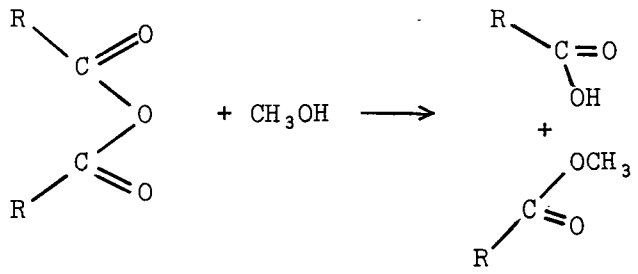
The products found from the oxidation of 4-methylveratrole (II) would indicate that this reaction follows much the same pathway as oxidation of 4-methylpyrocatechol. Since it is an "ortho-dioxy" compound like the catechol, it presumably can also be oxidized to the o-quinone (XIII). Subsequent reactions would follow as described earlier:



II XIII

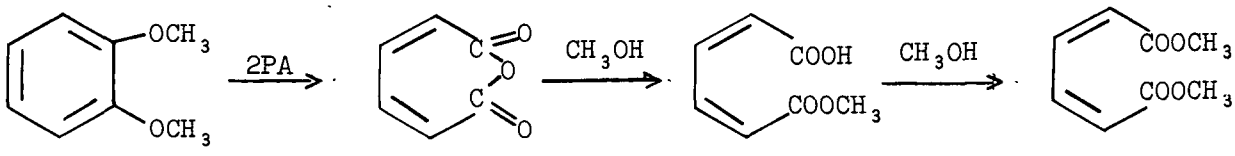
The fact that no methyl esters of these products were found shows that some intermediate such as an o-quinone must be formed to remove the methyl groups.

The recovery of muconic acid methyl esters from methoxy-aromatic structures reported earlier (27, 30, p. 45) seems to contradict the existence of an o-quinone intermediate. However, if o-quinone formation did occur, methanol would probably be initially released. Since an anhydrous organic solvent was used, any anhydride subsequently formed could only open by combining with the methanol:



This would give one methyl ester and explain the methoxynaphthalene result.

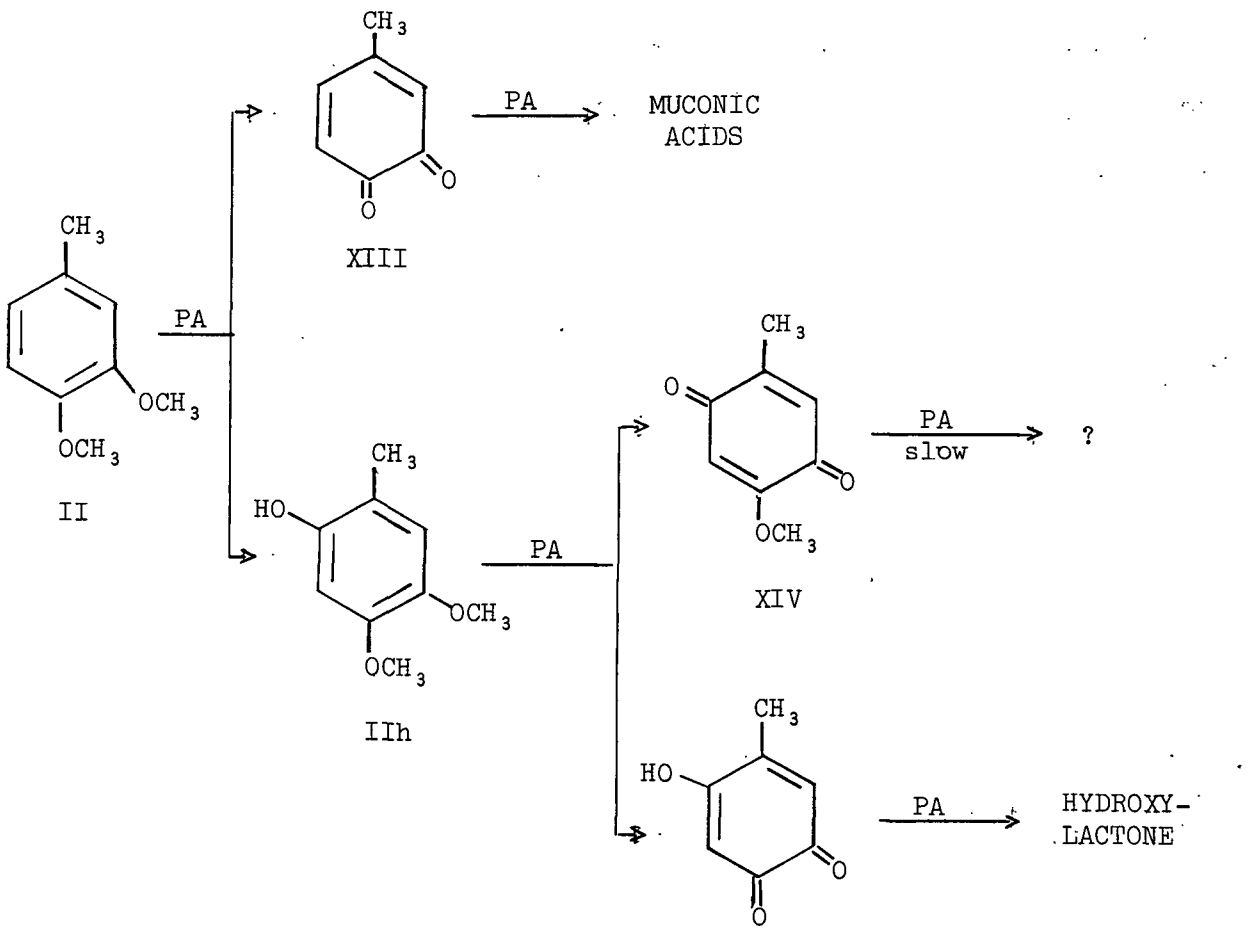
However, this would not explain the dimethylmuconate found from the 1,2-dimethoxybenzene oxidation. Monomethylmuconate could form as above but subsequent esterification by methanol would have to occur to give the dimethyl ester:



Therefore, the methyl ester products found in these two studies don't necessarily contradict the proposed o-quinone intermediate.

Another mode of peroxyacid attack would be hydroxylation at the C-5 position on the ring, giving 5-hydroxy-4-methylveratrole (IIh). Further oxidation at the orthomethoxyl positions would form a hydroxy-o-quinone and finally result in the γ-hydroxy-lactone. However, the hydroxylated starting material can apparently also react at the C-2 methoxyl and C-5 hydroxyl positions to yield the p-quinone product (XIV) found. In this case, formation of the p-quinone would appear to be the faster reaction because much more p-quinone was present in the product than γ-hydroxy-lactone (17 and 1%, respectively).

Thus, an overall reaction scheme can be written for 4-methylveratrole as follows:



Except for formation of the p-quinone, this reaction sequence is identical to that proposed for 4-methylpyrocatechol.

The stoichiometry results, however, were not as easily explained. The oxidation of 4-methylveratrole to either the p-quinone or to muconic acids requires two moles of peroxyacid while formation of γ-hydroxy-lactone would consume three moles. Based on the product yields in Table XV, a stoichiometry of 2.04 would be predicted at ∿ 80% reaction. This is considerably lower than the experimental result of 2.9. The increase in stoichiometry as a function of reaction time cannot be explained easily by the products either.

The increasing stoichiometry could result from further slow oxidation of some initial products. Although the muconic acids have been shown to be stable to peroxyacetic acid, the p-quinone was found to react. When 0.43 g. of 2-methoxy-5-methyl-p-benzoquinone was mixed with 25 ml. of 7% peroxyacetic acid, only 0.16 g. (36%) reacted in 50 hours, with a stoichiometry slightly greater than 1.0. The reaction mixture was worked up and analyzed, but no products were found. Thus, although this secondary reaction would result in a total requirement of > 3.0 moles of peroxyacid, its slow rate would account for only a small part of the rising stoichiometry. It would also be a minor cause of the difference between predicted and experimental stoichiometry.

The methoxyl groups present in the starting material might also be responsible for the high stoichiometry. Formation of a p-quinone or o-quinone would cause the loss of one or two methyl groups, respectively, giving methanol and/or methyl acetate. However, methanol was found to be unreactive in peroxyacetic acid and methyl acetate would probably only be oxidized by larger concentrations of hydrogen peroxide.

Another possibility would be oxidative removal of one of the methoxyl groups in addition to a hydrolytic, nonoxidative loss of the other methoxyl. This would raise the theoretical stoichiometry requirement of the muconic acids and p-quinone from 2.0 to 3.0. Therefore, a minimum initial stoichiometry of 3.0 would be expected, which does not agree with the experimental results.

Thus, the most likely remaining possible cause of both the increase in stoichiometry and resulting high value would be the two-thirds of the product that was not found.

OXIDATION OF p-CRESOL

PRODUCTS

Neutral Products

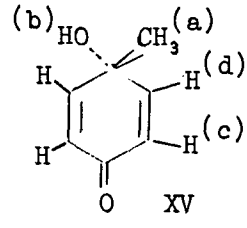
Reports in the literature (22, 25, 47) of the peroxyacetic acid oxidation of p-cresol make no mention of products other than carboxylic acids. However, in this study two neutral, noncarboxylic products were found. One product was present only in small amounts and was not isolated or identified. This unknown was denoted U5.

The main noncarboxylic product from the p-cresol oxidation was isolated by GLC and found to be 4-hydroxy-4-methyl-2,5-cyclohexadienone (XV). This will be referred to as the "dienone." Rigorous identification was accomplished by infrared, NMR, and mass spectra analyses, as reported in Tables XVII and XVIII. This compound has been reported in the literature as a product of the oxidation of p-cresol by aqueous hydrogen peroxide (66). The (c) and (d) protons in Table XVII constitute an $A_2'B_2'$ pattern. The chemical shifts were calculated as for an AB pattern (49).

TABLE XVII

SPECTRAL DATA FOR 4-HYDROXY-4-METHYL-2,5-CYCLOHEXADIENONE (DIENONE)

Infrared[a]		NMR ($CDCl_3$)				
cm.$^{-1}$	Assignment	δ, p.p.m.	Multiplicity	J, Hz	Number of Protons	
3400 (MS)	OH	1.48 (a)	1	--	3	
3040 (W)	=C-H	3.07 (b)	broad	--	1	
2980 (MW)	$-CH_3$	6.13 (c)	2	10	2	$A_2'B_2'$
1660 (S)	C=O	6.96 (d)	2	10	2	
1630 (MS)	C=C					
1617 (MS)	C=C					
856 (S)	=C-H					



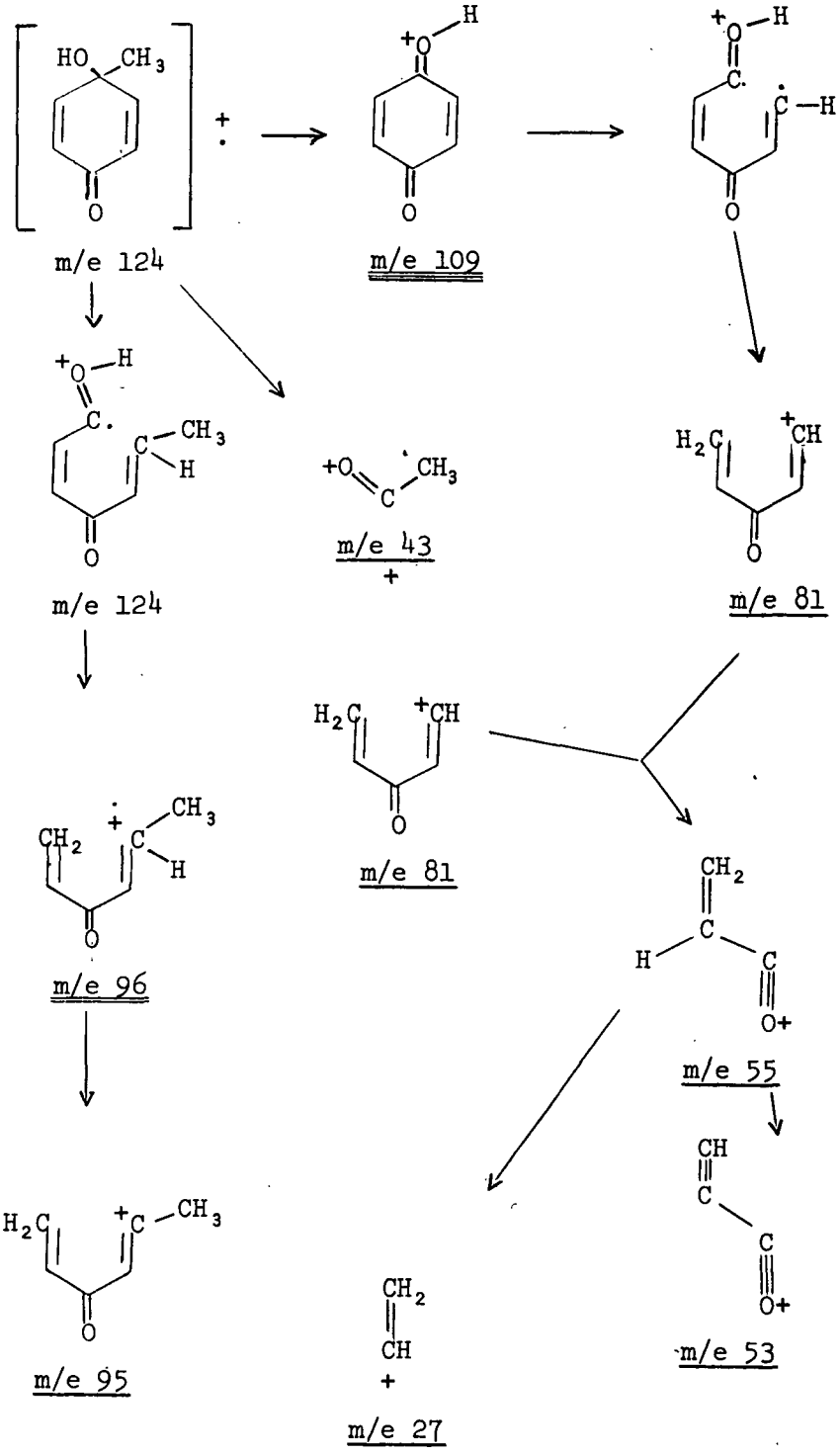
XV

[a] Liquid between NaCl plates.

TABLE XVIII

MASS SPECTRUM OF 4-HYDROXY-4-METHYL-2,5-CYCLOXADIENONE AND INTERPRETATION (DIENONE)

m/e	% of Base	
126	0.4	(P+2)
125	4	(P+1)
124	33	(P)
123	2	
110	8	
109	100	(Base)
108	14	
107	16	
97	7	
96	46	
95	23	
82	9	
81	58	
79	9	
78	8	
77	18	
70	4	
69	14	
67	9	
66	3	
63	5	
55	23	
54	12	
53	33	
52	13	
51	19	
50	10	
43	36	
42	8	
41	12	
40	5	
39	19	
38	5	
29	7	
28	9	
27	28	
26	14	
18	24	
17	6	
15	8	



The NMR and infrared spectra give very clear-cut evidence for this structure. The NMR pattern shows two identical sets of vinyl hydrogens (c+d). This indicates that the molecule contains a plane of symmetry. The structure must also be cyclic because the only other hydrogens present are in the methyl (a) and hydroxyl (b) groups. Thus, adding the ketone (conjugated) group found from the infrared and the hydroxyl and methyl groups, Structure XIV is the only one possible. This structure follows logically from the starting material, p-cresol.

Derkosch and Kaltenegger (67) carried out an infrared study of some cyclohexadienones. The following bands reported for 4,4-dimethylcyclohexadien-1-one are very similar to those found in the dienone spectrum in Table XVII: 1668 (C=O), 1635 (C=C), 1601 (C=C), and 859 $cm.^{-1}$ (=C-H).

The mass spectrum of the dienone further confirms this structure, showing a strong parent peak at m/e 124. A lower energy spectrum resulted in a large increase in the m/e 124 peak relative to the base peak (m/e 109), thus confirming the parent peak. Much of the subsequent fragmentation pattern follows previous findings (68). The base peak, m/e 109, results from loss of the methyl group. This cyclic ion can break down further, losing carbon monoxide, and form a linear dienone at m/e 81. The molecular ion can also break down by losing an acetyl ion (m/e 43) which would give the linear dienone. The other main mode of fragmentation evidently results from migration of the methyl group in the molecular ion. This enables loss of carbon monoxide to give the m/e 96 fragment.

The other neutral compound found in the p-cresol oxidation product (after reduction of excess peroxyacid by acetaldehyde) was collected and identified as 6,8-dimethyl-3-keto-$\Delta^{4,5}$-7,9-dioxabicyclo[4.3.0]nonane (XVI). This will be referred to as the dienone-acetal product in future discussions. The spectral data for this product are listed in Tables XIX and XX.

TABLE XIX

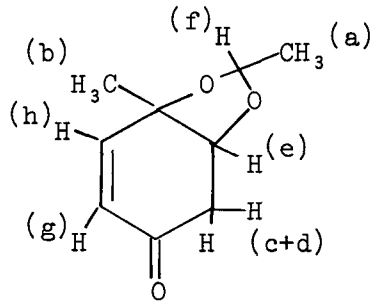
SPECTRAL DATA FOR 6,8-DIMETHYL-3-KETO-$\Delta^{4,5}$-7,9-DIOXABICYCLO[4.3.0]NONANE (DIENONE-ACETAL)

Infrared[a]		NMR ($CDCl_3$)				
cm.$^{-1}$	Assignment	δ, p.p.m.	Multiplicity	J, Hz	Number of Protons	
2980 (M)	CH_3	1.35 (a)	2	5	3	
2930 (W)	CH_2	1.53 (b)	1	--	3	
2880 (M)	CH_3	2.58 (c)	4	18,3	1	ABX
1680 (VS)	C=O	2.88 (d)	8	18,3,1	1	ABX
1130 (VS)	C-O	4.19 (e)	5	2.5	1	ABX
		5.08 (f)	4	5	1	
		6.07 (g)	4	10,1	1	AB
		6.48 (h)	4	10,2	1	AB

[a]Liquid between NaCl plates.

COUPLINGS FOUND FROM DECOUPLING EXPERIMENTS

(a) ↔ (f)
(h) ↔ (e)
(e) ↔ (c+d)

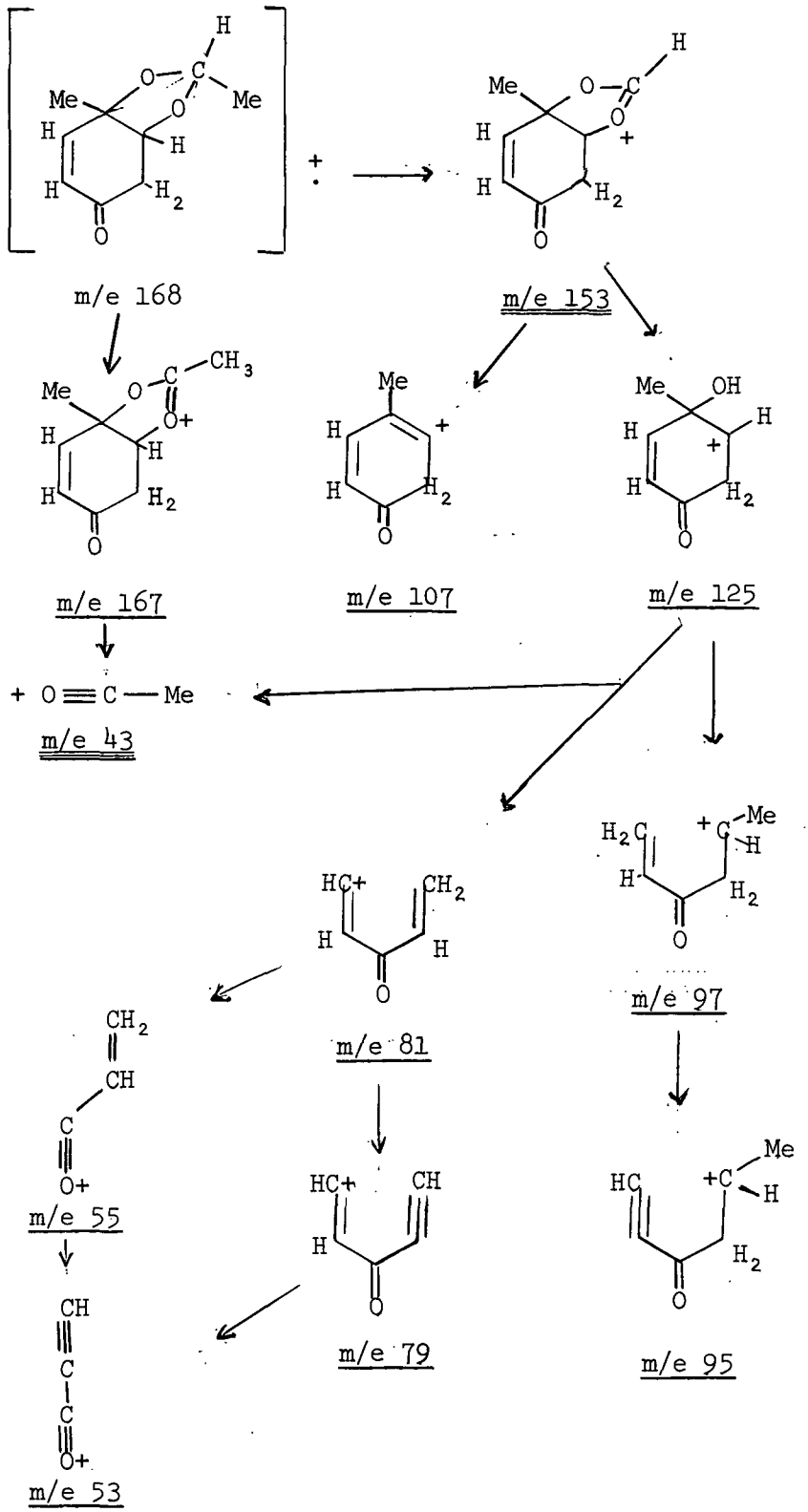


XVI

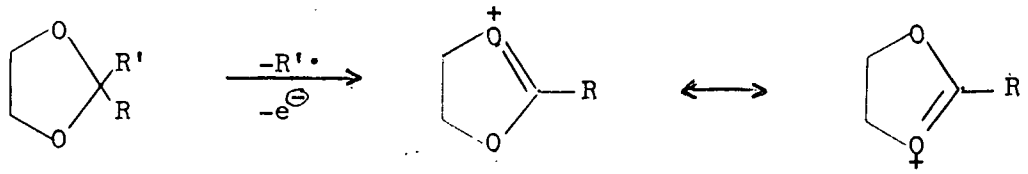
TABLE XX

MASS SPECTRUM OF 6,8-DIMETHYL-3-KETO-$\Delta^{4,5}$-7,8-DIOXABICYCLO [4.3.0]NONANE (DIENONE-ACETYL) AND INTERPRETATION

m/e	% of Base	
170	0.1	(P+2)
169	0.3	(P+1)
168	1	(P)
167	4	
154	9	
153	90	
126	4	
125	42	
109	12	
107	23	
98	5	
97	30	
96	5	
95	33	
83	5	
82	8	
81	24	
80	7	
79	38	
77	10	
71	10	
69	8	
67	7	
55	18	
54	9	
53	23	
52	7	
51	7	
45	16	
44	5	
43	100	(Base)
42	5	
41	20	
39	14	
29	9	
28	10	
27	24	
26	5	
18	5	
15	10	



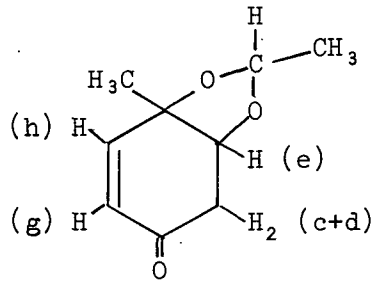
The parent peak in the mass spectrum was very weak. A lower voltage spectrum resulted in a slight increase of the m/e 168 peak relative to the 167 peak, indicating that m/e 168 was the molecular ion. Also, since no nitrogen atoms are present in these products, the parent peak has to have an even mass. A fundamental fragmentation result in acetal compounds is loss of an "R" group from the acetal carbon (69):



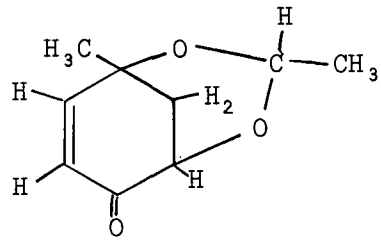
Thus, a hydrogen radical must be lost from the acetal group to give the m/e 167 peak (P-1). Similar loss of a methyl radical would give the m/e 153 ion, which is second only to the base peak in intensity. The acetal, after loss of the methyl radical, can evidently lose a mole of formic acid or carbon monoxide to form the indicated ions. The m/e 125 ion is then similar to the dienone previously discussed and breaks down accordingly, giving the base peak at m/e 43.

The NMR spectrum points out the coupled methyl and hydrogen on the acetal carbon (a and f). The methyl group (b) on the ring gives a singlet and the correct chemical shift for being adjacent to an oxygen linkage. Bands (c) and (d) are due to methylene hydrogens and constitute the AB portion of an ABX pattern; (e) is the adjacent hydrogen (X) next to an oxygen atom. The true chemical shifts for the AB protons (c and d) were calculated (50). Finally, the vinyl hydrogens (g) and (h) were determined from literature data (52). The couplings listed in Table XIX were determined by "double-resonance" decoupling experiments.

From these data there appeared to be two possible structures, XVI and XVIa:



XVI



XVIa

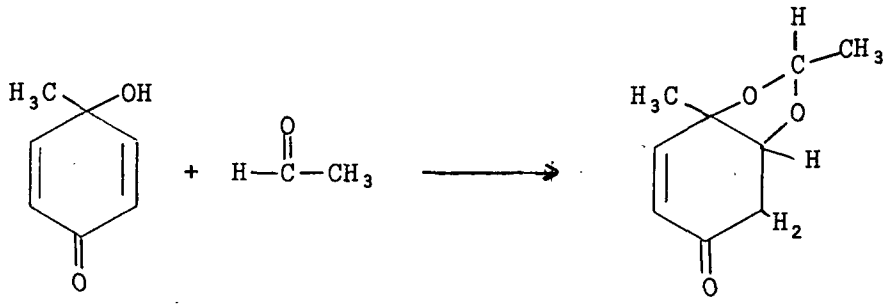
However, the long-range coupling present showed that XVI must be the correct structure. The methylene protons (c+d) were apparently coupled to the proton (g) adjacent to the ketone group. The other vinyl proton (h) was found to be coupled with the methine proton (e). Thus, Structure XVI fits these results best.

The low frequency of the ketone infrared band indicated conjugation. Several carbon-oxygen bonds were also indicated by the very strong band at 1130 $cm.^{-1}$ Therefore, all of the spectral data supports the acetal structure, XVI.

It was later discovered that the acetal product was formed during the peroxyacid reduction step in the product work-up. When the p-cresol oxidation product was not mixed with acetaldehyde to reduce the peroxyacid, no acetal was found. As a result, the yield of dienone was found to increase.

To verify this, the dienone (10 mg.) was mixed with 1.1 ml. of 5% peroxyacetic acid solution. A sample of the solution was injected on the gas chromatograph, giving the dienone peak. Acetaldehyde (0.3 ml.) was then added, and after 30 minutes, another sample was injected, giving the dienone peak and a small peak for the acetal. More acetaldehyde was added (0.2 ml.) and an injection made after another 30 minutes showed the presence of more acetal and less dienone.

After being stored one day, GLC analysis showed that even more acetal had been formed. Since the reduction of peroxyacetic acid should have been finished in the first 30 minutes, the reaction taking place is evidently a simple combination of acetaldehyde with the dienone (XV). The discovery of this reaction is



XV XVI

more evidence that the proposed dienone-acetal (XVI) structure is the correct one.

Since the acetal was not an oxidation product, the amount of this material found in worked-up product mixtures was converted into grams of dienone as explained in Appendix VI. Therefore, the results in Table XXI show only the yields of the dienone and unknown, U5, from the ether extract product.

Carboxylic Acid Products

All four carboxylic acids identified from the 4-methyl-pyrocatechol oxidation were also found in the p-cresol oxidation product: β-methylmuconic acid, β-methyl-lactone, γ-methyl-lactone, and γ-hydroxy-lactone. These were all positively identified by collecting the methyl esters and comparing their infrared spectra with those of the authentic compounds. The quantitative results are reported in Table XXI.

The presence of β-methylmuconic acid and a lactone acid as products of the p-cresol oxidation with peroxyacetic acid has been known for some time (22, 47). However, the actual structure of the lactone acid was not shown to be β-methyl-lactone until later (25).

TABLE XXI

PRODUCT YIELDS FROM p-CRESOL OXIDATION

Reaction No.	Reaction Time, hr.	Reaction, %	Product Yield, % of theoretical					H_2O_2, %
			Dienone	U5	Muconic Acids	Hydroxy[a] Lactone	Total	
2629-102	68	74.2	13.5	1.1	N.D.[b]	N.D.	N.D.	0.1
2675- 13-4	57	71.2	7.8	0.6	42.6	5.6	56.6	0.09
87-4	54	70.6	18.8	0.6	28.7	3.5	51.6	0.30
155-3[c]	54	69.4	15.9	0.6	N.D.	N.D.	N.D.	0.05
2617- 80[c,d]	63	71.3	10.3	1.3	23.2	3.8	38.6	0.2
90-3[d]	56	72.3	4.8	0.5	33.7	4.1	43.1	0.28
Averages			11.9	0.8	32.1	4.3	49.1	

Reaction No.	Muconic Acids, % of theoretical				
	γ-ML (VIII)	β-ML (VII)	U2	β-MMA (VI)	U3+U4
2629-102	N.D.	N.D.	N.D.	N.D.	N.D.
2675- 13-4	2.6	25.6	11.1	--	3.3
87-4	2.5	16.1	9.1	--	1.0
155-3[c]	N.D.	N.D.	N.D.	N.D.	N.D.
2617- 80[c,d]	2.6	17.3	22.8	0.5	--
90-3[d]	2.7	18.5	7.8	0.5	4.2

[a] γ-Hydroxy-lactone results approximated from other data.

[b] N.D. = not determined.

[c] Reaction run in presence of methyl methacrylate.

[d] Remaining peroxyacid solution not reduced.

The hydrogen peroxide content in the reaction solutions studied was kept low (< 0.3%) and thus should have had a negligible effect.

STOICHIOMETRY

Table XXII reports the stoichiometry results found from the p-cresol oxidation by peroxyacetic acid. The recovery of p-cresol in the work-up procedure used in stoichiometry runs was found to be complete. Also, none of the identified products should interfere in the peroxyacid titration. The hydrogen peroxide present in these stoichiometry runs should have had no effect, since a very low concentration was present.

TABLE XXII

p-CRESOL STOICHIOMETRY

Reaction No.	Reaction Time, hr.	Reaction, %	Stoichiometry	H_2O_2, %
2601-106-1	6.5	21.2	2.76	0.05
106-2	16.5	39.9	2.77	0.05
106-3	20.5	51.8	2.81	0.05
106-4	40.5	60.6	2.77	0.05
2675- 13-4	57	71.2	2.53	0.09
70-1	48.5	66.3	2.64	0.03
155-3[a]	54	69.4	2.78	0.05

[a]Run in presence of methyl methacrylate; stoichiometry approximate because control correction was estimated.

Fresh peroxyacetic acid was prepared for each oxidation noted in Table XXII (Reactions 106-1 — 106-4 were made up from the same peroxyacid solution). Since each batch of peroxyacid prepared has a slightly different composition (water,

acetic acid, and hydrogen peroxide content vary), this could be one reason for the variation in stoichiometry results.

The results of the product analyses in Table XXI generally agree with the stoichiometry findings. Oxidation of p-cresol to the dienone would require only one mole of peroxyacid. Oxidation to muconic acids would consume three moles and to the γ-hydroxy-lactone, four moles of peroxyacid. Therefore, based on the average yields found in Table XXI, a stoichiometry of 2.60 would be predicted, which lies within the range of stoichiometries found. This indicates that the other half of the products not detected required about the same amount of oxidant as those that were identified.

A very important result is the constant stoichiometry of the p-cresol oxidation with degree of reaction. This is shown in the first four runs (2601-106-1 to -106-4). This indicates that all of the oxidation products (both detected and undetected) are stable in the presence of peroxyacetic acid.

METHYL METHACRYLATE EFFECT

As mentioned in the introduction, there is some evidence to indicate that free radicals are not present in peroxyacid oxidations run in the absence of free-radical initiators (31). Methyl methacrylate, an excellent free-radical scavenger, was added to several p-cresol oxidation reactions to determine whether any change in the reaction would occur. At the end of these reactions, the solutions were diluted with water but no polymer precipitated. If free radicals had been present, methyl methacrylate would have polymerized and precipitated after dilution. Subsequent product and stoichiometry analysis results given in Tables XXI and XXII show that methyl methacrylate had no significant effect.

In addition, it was found that methyl methacrylate had no effect on the rate of consumption of peroxyacetic acid in a p-cresol oxidation. Table XXIII gives the titration data for two p-cresol oxidations (after correction for dilution by methyl methacrylate), one containing 3% methyl methacrylate. As can be seen, the peroxyacid was consumed in both reactions at almost exactly the same rate.

TABLE XXIII

EFFECT OF METHYL METHACRYLATE (MeMac) ON RATE OF PEROXYACETIC ACID CONSUMPTION

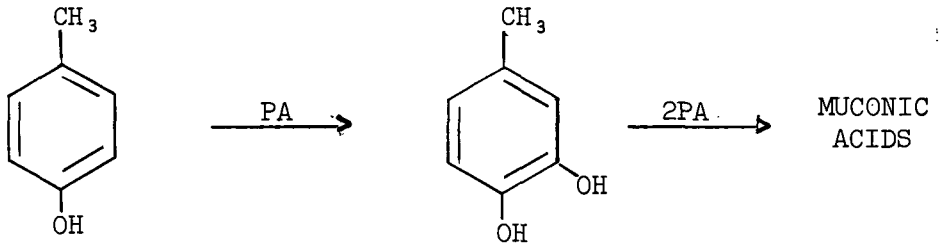
Reaction Time, hr.	Peroxyacetic Acid, %	
	p-Cresol Control	p-Cresol + MeMac
0	9.78	9.78
3.8	8.89	8.68
8.8	7.57	7.61
14.6	6.54	6.63
20.7	5.78	5.84
27.9	5.09	5.13
36.5	4.46	4.47
46.1	3.95	3.93
54.3	3.61	3.57

Therefore, the fact that methyl methacrylate had no effect on any aspect of the p-cresol oxidation is excellent evidence that the oxidation mechanism is not free radical.

The reductions of peroxyacetic acid by acetaldehyde and by sodium bisulfite were studied in the presence of methyl methacrylate. Dilution with water at the end of the reaction caused a considerable amount of polymer to precipitate. Infrared analysis proved this to be polymethyl methacrylate, indicating that these rapid reactions are free radical.

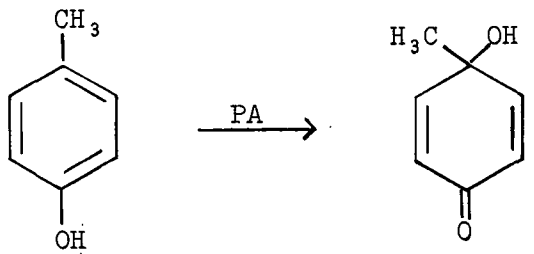
OXIDATION MECHANISM

The same muconic acids were found from the p-cresol oxidation as from the previous two substrates discussed. Thus, a similar oxidation mechanism is probably involved. However, an additional initial oxidation would be required since only one oxygen-containing substituent is present in the starting material. An initial reaction could be hydroxylation ortho to the original hydroxyl, giving 4-methylpyrocatechol, whose oxidation mechanism has already been discussed. Since the

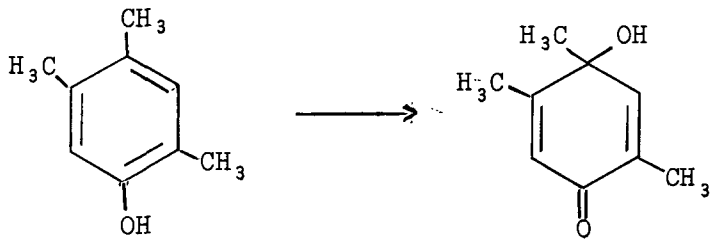


reactivity of the catechol substrate is much greater than that of p-cresol, the rate-determining step would have to be the initial hydroxylation.

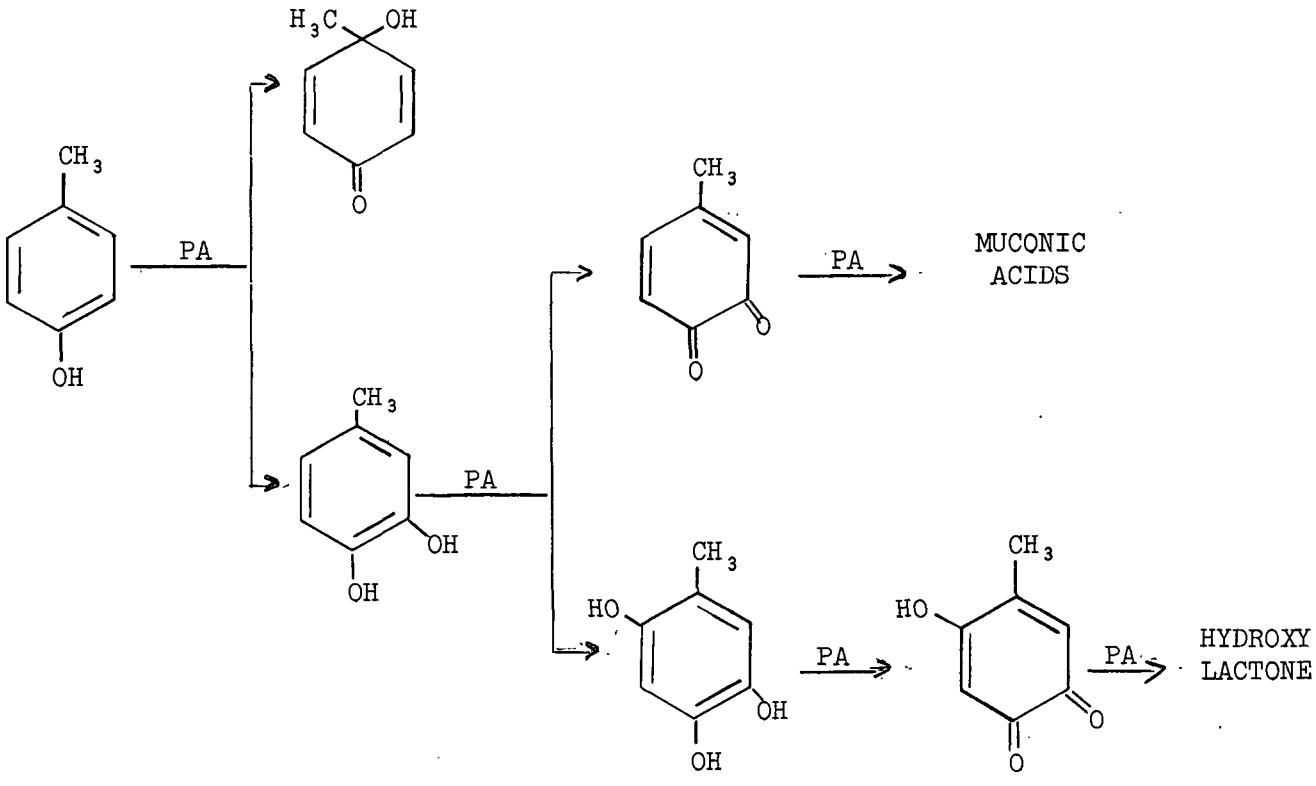
Hydroxylation at the C-1 position evidently results in formation of the dienone product:



Chambers, et al. (21) studied the oxidation of 2,4,5-trimethylphenol by trifluoroperoxyacetic acid and also found a dienone product (10%):



From the above results, an overall reaction sequence can be constructed for the p-cresol oxidation:



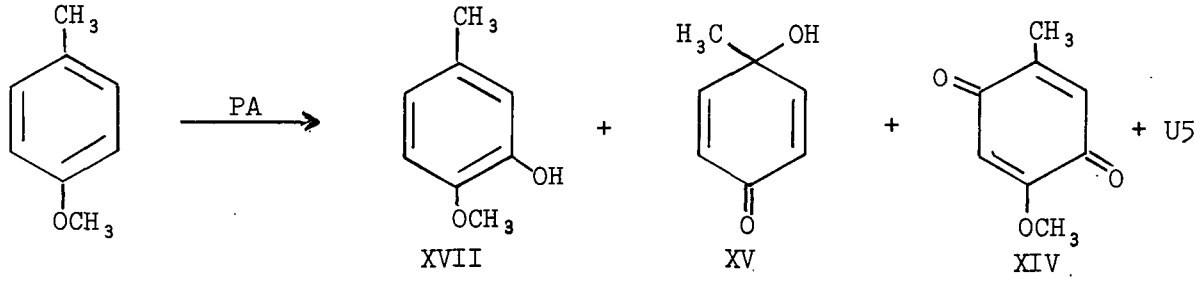
This figure describes the two possible hydroxylation reactions competing at the beginning of the oxidation. The stability of the dienone product, shown by the constant stoichiometry, demonstrates the effect of conjugation in "deactivating" otherwise reactive olefin and carbonyl groups (10, 18).

OXIDATION OF p-METHYLANISOLE

PRODUCTS

Neutral Products

Five compounds were found in the worked-up initial ether extract of the p-methylanisole oxidation: the dienone (XV), acetal (XVI), and unknown U5 found from p-cresol; the p-quinone (XIV) found from 4-methylveratrole, and one new product, 2-hydroxy-p-methylanisole (XVII). This last product was collected by GLC, and its infrared spectrum was identical to a spectrum of the authentic material (70). The product yields are shown in Table XXIV. The amount of acetal found in each product mixture was converted to grams of dienone (Table L). Thus, the oxidation of p-methylanisole results in four volatile products:



Carboxylic Acid Products

The carboxylic acid products found from this reaction were the same ones found from all previous oxidations: γ-methyl-lactone, β-methyl-lactone, γ-hydroxy-lactone, and β-methylmuconic acid. The yields of these products are given in Table XXIV.

Oxidations run in the presence of 1-1.4% hydrogen peroxide caused no obvious change in the yields of volatile products. However, negligible amounts of muconic acids resulted while a new product, U2A, was found. This new unknown was not collected or identified. Furthermore, its significance is doubtful, since its retention time coincides with an unknown product found from the work-up of a peroxyacetic acid-acetaldehyde control reaction.

TABLE XXIV

PRODUCT YIELDS FROM p-METHYLANISOLE OXIDATION[a]

Reaction No.	Reaction, %	Product Yield, % of theoretical: 2-Hydroxy-p-MA	Dienone	U5	p-Quinone	Muconic Acids	Hydroxy-Lactone[b]	U2A	Total	H_2O_2, %
2675 -25-1	24.6	5.6	24.2	--	--	10.5	1.6	--	41.9	0.34
87-1	25.5	6.6	19.8	1.0	--	12.7	1.9	--	42.0	0.30
25-2	44.0	1.6	14.1	1.5	18.5	16.5	2.0	--	54.2	0.34
87-2	45.7	2.5	15.3	1.7	8.1	13.0	1.9	--	42.5	0.30
155-1	44.3	2.7	18.4	1.7	11.5	N.D.[c]	N.D.	N.D.	N.D.	0.05
2629- 97	47.4	2.3	16.7	2.7	24.5	N.D.	N.D.	N.D.	N.D.	0.1
2675-128	55.5	1.9	12.7	1.8	15.2	1.5	--	0.6	33.7	0.99
2617- 71	48.7	2.2	18.2	2.1	11.2	2.5	0.1	1.0	37.3	1.41
Averages[d]		2.3	16.1	1.8	15.7	14.8	2.0	--	52.7	

Reaction No.	Muconic Acids, % of theoretical: γ-ML (VIII)	β-ML (VII)	U2	β-MMA (VI)	U3+U4
2675- 25-1	0.9	6.1	2.9	--	0.6
87-1	1.0	7.1	2.7	--	1.9
25-2	1.2	7.5	4.6	0.1	3.1
87-2	0.9	7.0	3.2	0.3	1.6
155-1	N.D.	N.D.	N.D.	N.D.	N.D.
2629- 97	N.D.	N.D.	N.D.	N.D.	N.D.
2675-128	--	--	0.8	0.7	--
2617- 71	0.2	0.2	2.1	--	--

[a] All oxidations run for about 72 hr. except 2675-25-1 (30 hr.) and 2675-87-1 (48 hr.).

[b] Hydroxy-lactone yield approximated from other data.

[c] N.D. = not determined.

[d] Average of middle four oxidations (2675-25-2 through 2629-97).

Control reactions of β-methylmuconic acid (0.1 g.) and β-methyl-lactone (0.6 g.) for 24 hours in 6.5% peroxyacid/1.5% hydrogen peroxide gave 33 and 67% yields, respectively, of β-methyl-lactone. Both figures are lower than yields reported earlier for similar controls run in the presence of < 0.3% hydrogen peroxide (47 and 79%, respectively). However, the muconic acid product yields in the 4-methylpyrocatechol oxidation products did not seem to change with higher peroxide content.

STOICHIOMETRY

In the quantitative analysis of p-methylanisole reaction products, incomplete recovery of remaining p-methylanisole occurred in a few cases. Therefore, it was necessary to correct two stoichiometry results in Table XXV. These results are reported as the original result followed by the corrected figure (underlined). This work-up problem is discussed in more detail in the experimental section. The use of a more efficient work-up method gave 96-97% recovery of p-methylanisole in the other reactions. These results were not corrected.

The results of Runs 117-1 through 117-4 show that the stoichiometry of the p-methylanisole oxidation increases with the degree of reaction. Also, significant in these results is the stoichiometry of 1.6 at early reaction time. This indicates that a high proportion of the initial oxidation results in formation of products that require a stoichiometry of 1.0.

TABLE XXV

p-METHYLANISOLE STOICHIOMETRY

Reaction No.	Reaction, %	Stoichiometry	H_2O_2, %
2601-117-1	7.5	1.65	0.25
157-2	8.8	1.68	1.1
117-2	19.6	2.11	0.25
117-3	25.3	2.42	0.25
117-4	33.1	2.74	0.25
2675-155-1[a]	53.2/44.3	2.53/3.04	0.05
2617-71[a]	56.9/48.6	2.46/2.87	1.41

[a]Results corrected for substrate lost in work-up.

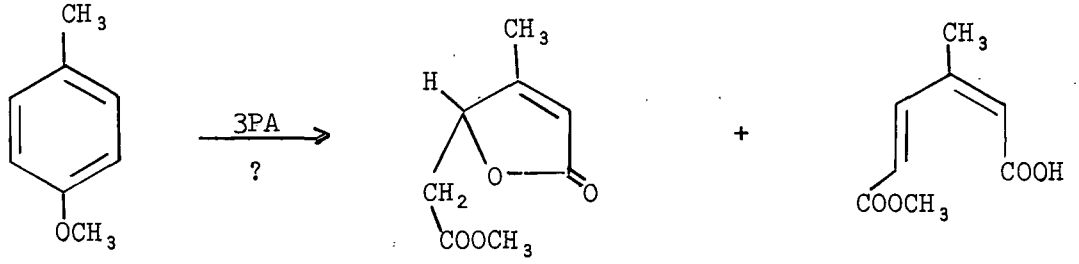
Oxidation of p-methylanisole to either the dienone or 2-hydroxy-p-methylanisole would require one mole of peroxyacid. Oxidation to muconic acids or the p-quinone would consume three moles of peroxyacid while the γ-hydroxy-lactone would require four moles. The predicted stoichiometry calculated from the average product yields determined in Table XXIV for ∿ 45% reaction would then be about 2.3. This is much lower than the experimental result of ∿ 3.0. To account for this difference, much of the approximately 50% of the product that was not formed would seem to be composed of products requiring three and four moles of peroxyacid.

The presence of a relatively large amount of hydrogen peroxide (2601-157-2 and 2617-71 in Table XXV) caused only a small apparent chang in the stoichiometry results. Thus, the effect of hydrogen peroxide is evidently negligible in concentrations lower than 0.3%.

OXIDATION MECHANISM

The mechanism of the p-methylanisole oxidation should be very similar to that proposed for p-cresol. Both substrates have one oxygen-containing substituent, and both oxidations result in nearly the same products. Thus, the first oxidation step would be peroxyacid attack ortho or para to the methoxyl group. Para attack results in formation of the dienone; ortho attack gives 2-hydroxy-p-methylanisole as a product. The discovery of this last product is convincing evidence for the hydroxylated intermediates that have been proposed. Thus, 2-hydroxy-p-methylanisole is evidently the intermediate that is oxidized to the o-quinone, from which the muconic acids are formed.

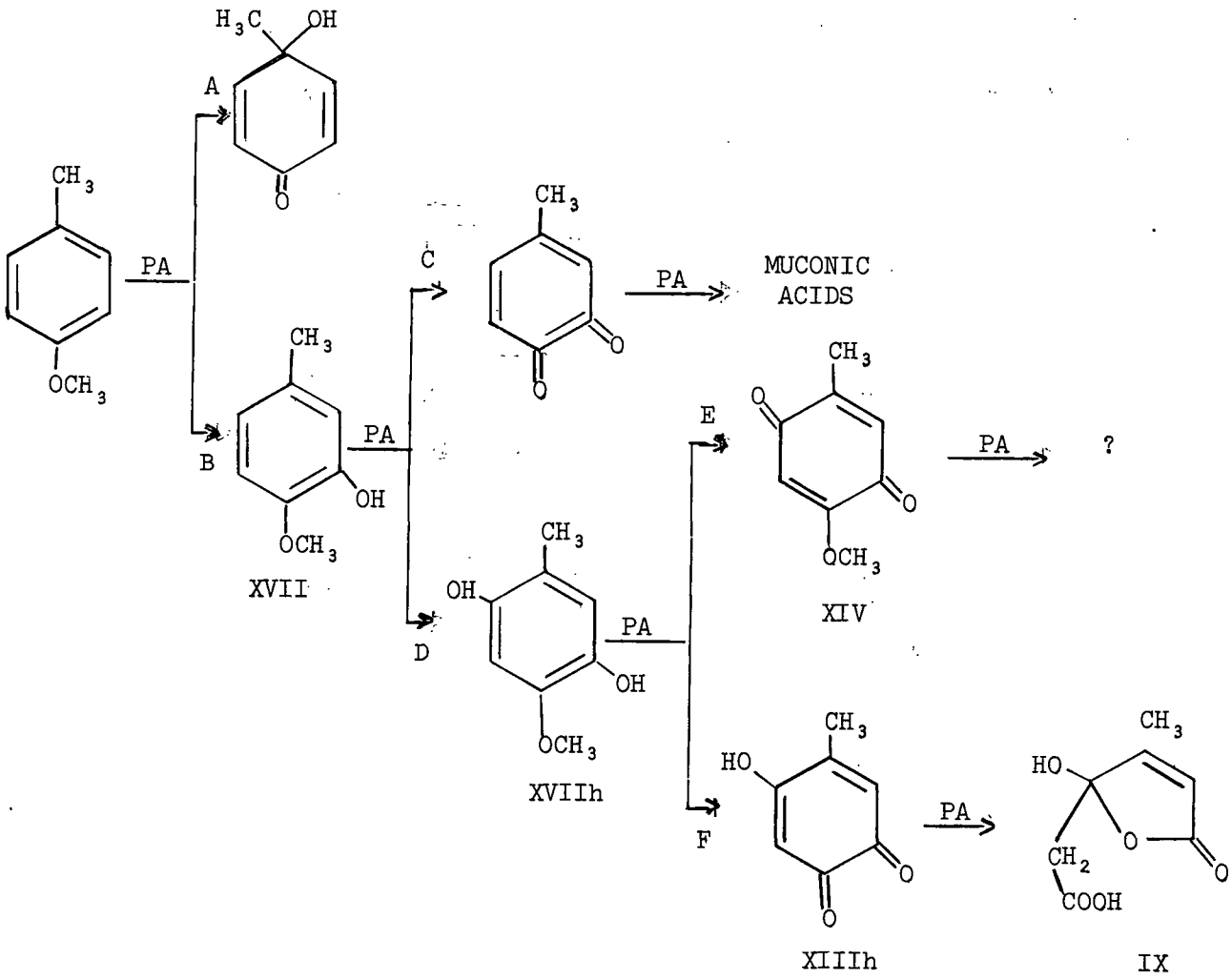
If an o-quinone was not an intermediate in this oxidation, it might be possible to retain the methoxyl group in the final muconic acids:



The β-methyl-lactone methyl ester (which was earlier shown to be stable in the oxidation solution) was sought in the p-methylanisole product mixture but was never found. Therefore, an intermediate such as an o-quinone must be responsible for loss of the methyl group.

Hydroxylation of 2-hydroxy-p-methylanisole at the C-5 position would give a para-dihydroxy compound (XVIIh) which could be oxidized to the p-quinone (XIV). The dihydroxy intermediate could also be oxidized to a hydroxy-o-quinone (XIIIh) from which the γ-hydroxy-lactone (IX) would be formed.

The entire reaction sequence just described can be written as follows:



The relatively low stoichiometry results at early reaction time can be explained by the corresponding higher yields of dienone and 2-hydroxy-p-methylanisole and the absence of p-quinone. This higher proportion of products that requires only one mole of peroxyacid for formation would give a lower stoichiometry. Clearly, Reactions A and B in the previous figure must predominate at early reaction times. However, as the oxidation proceeds, Reactions D and/or E become more important, giving a 15% yield of p-quinone at 45% reaction. The corresponding yields of dienone and 2-hydroxy-p-methylanisole were lower, and thus, a higher stoichiometry would be expected at longer reaction times.

Oxidation of the p-quinone product may also account for some of this change. In the 4-methylveratrole oxidation, the effect of further oxidation of the p-quinone product was not believed to be great because the reactions were only run 30 hours. However, the p-methylanisole oxidations were run for up to 72 hours, and the peroxyacetic acid concentration at the end of the reaction was always greater than 4%. This should offer ample opportunity for oxidation of the p-quinone product. Therefore, based on the results of the p-quinone oxidation control (p. 50) as much as one-half (0.1 g.) of the p-quinone product could have reacted in the p-methylanisole oxidation solution. If this is included with the average yields in Table XXIV, a stoichiometry of about 2.7 would be predicted. Thus, oxidation of the p-quinone product in the p-methylanisole oxidation could have been responsible for the majority of the difference between experimental and predicted stoichiometry. This also would have been a major cause of the increasing stoichiometry with time.

OXIDATION OF 2-METHOXY-p-CRESOL

A brief study was carried out on the peroxyacetic acid oxidation of 2-methoxy-p-cresol (XVIII). The product yields and stoichiometry results for the one reaction studied are given in Table XXVI.

The muconic acid products formed from 2-methoxy-p-cresol would require two moles of peroxyacetic acid while the hydroxy-lactone would require three. Calculating accordingly, a stoichiometry of 2.4 is predicted, which is much lower than the experimental result of 3.0. Therefore, the 60% of the products that was not accounted for must contain products whose formation requires three and four moles of peroxyacid. No neutral products were found.

TABLE XXVI

RESULTS OF 2-METHOXY-p-CRESOL OXIDATION

84.7% Reaction (24.3 hr.); 0.12% H_2O_2

Product Yields, % of theoretical			
Muconic Acids	Hydroxy-Lactone[a]	U2A	Total
19.9	13.4	8.1	41.4

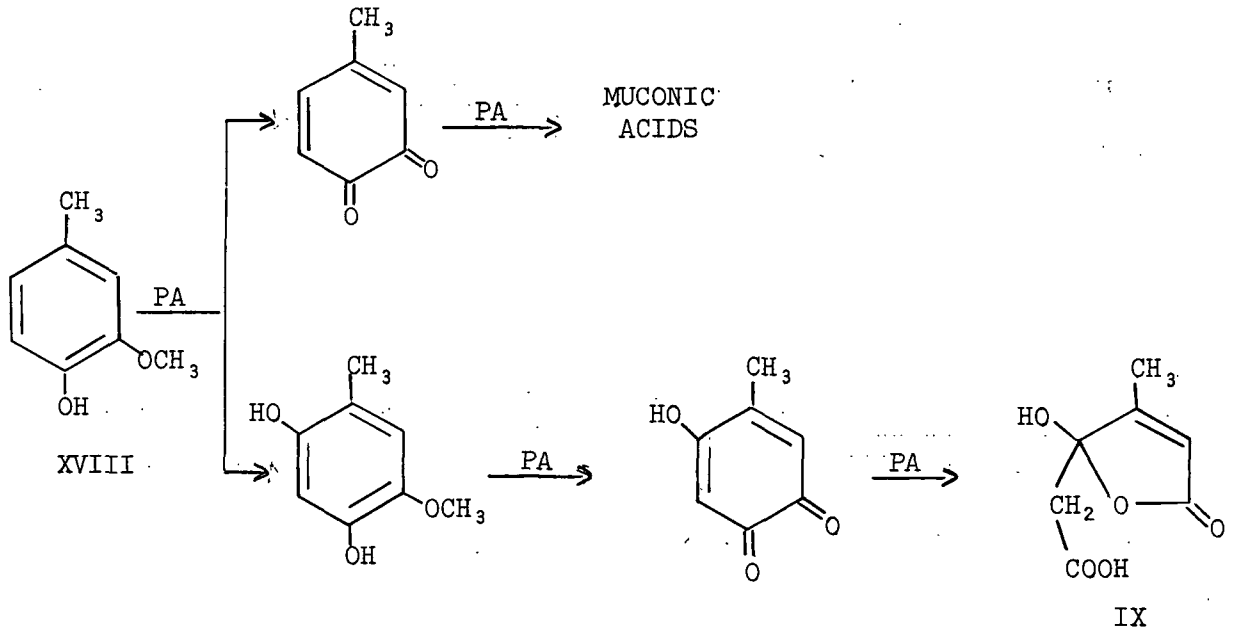
Stoichiometry = 3.02

Muconic Acids, % of theoretical				
γ-ML (VIII)	β-ML (VII)	U2	β-MMA (VI)	U3+U4
1.7	9.4	6.7	0.4	1.7

[a]Hydroxy-lactone yield approximated from other data.

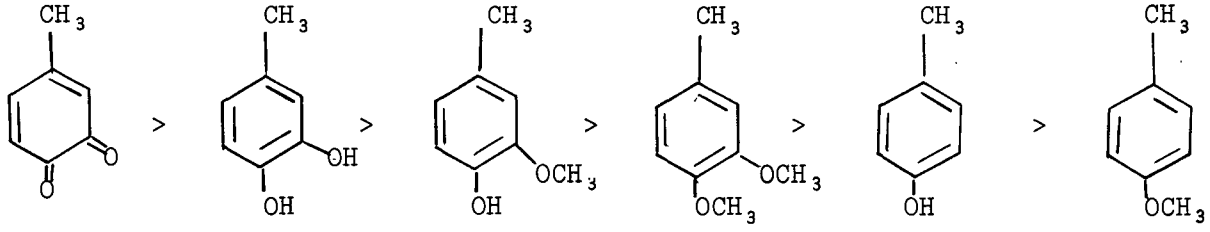
The significance of unknown peak, U2A, is not known, since it was found only in the 2-methoxy-p-cresol oxidation product and was not isolated or identified. The amount of γ-hydroxy-lactone formed was several times larger than from any other oxidation. The mechanistic implications of this high yield will be discussed in the next section.

The products found from the 2-methoxy-p-cresol (XVIII) oxidation, with the exception of U2A, are the same ones found in all previous oxidations. Also, there was no evidence for any methyl esters in the product, such as the methyl ester of γ-methyl-lactone. This ester might be formed if an o-quinone was not an intermediate in the oxidation to the muconic acids. Thus, the following oxidation sequence can be proposed:



SUMMATIVE DISCUSSION OF OXIDATION PATHWAYS

The relative reactivities of the various substrates studied were as follows:



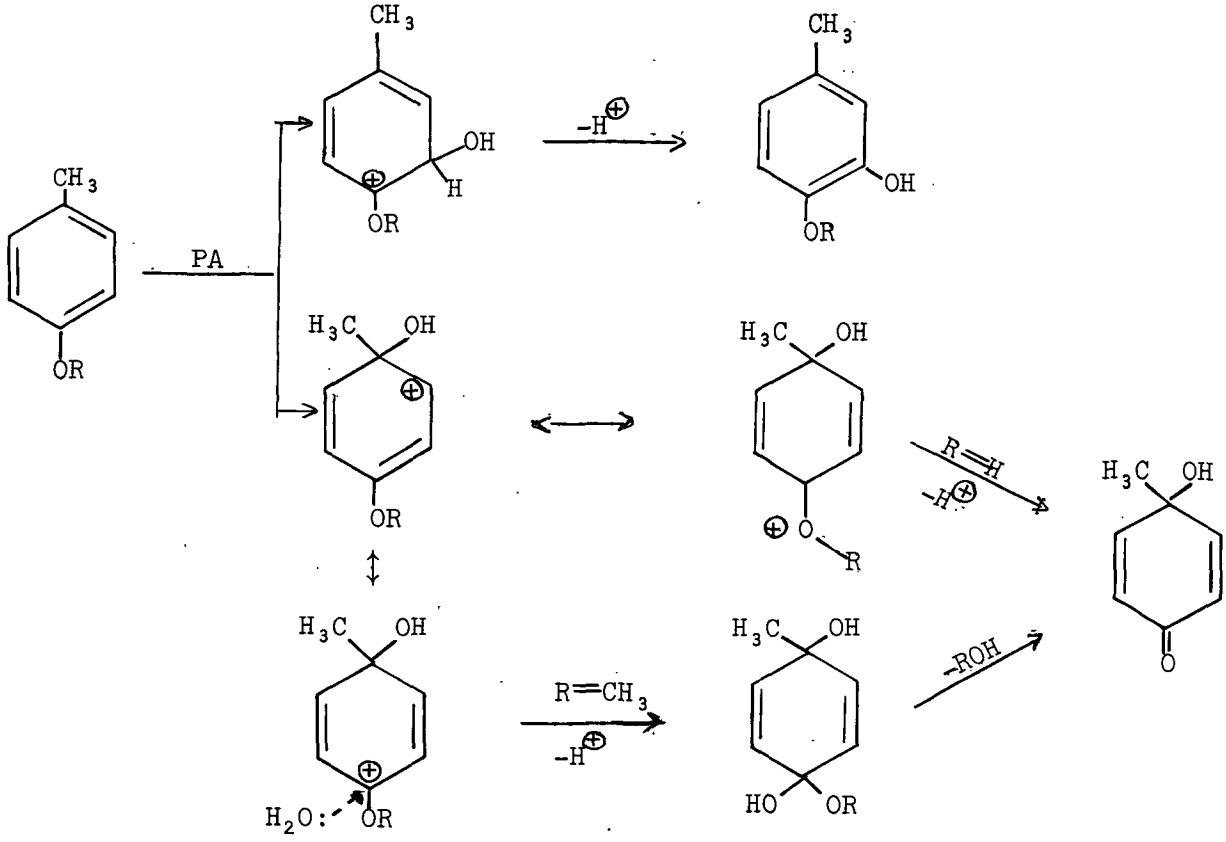
Approximate Half Lives (hr.) @ 25° :	0.01	0.2	4	5	25	100

These results point out two basic facts of the peroxyacetic acid oxidation of hydroxy- and methoxy-substituted aromatic compounds. The first is that an aromatic ring with two oxygen-containing substituents reacts faster (at least five times) than a ring having only one, whether hydroxyl or methoxyl. Secondly, the presence of a hydroxyl group on the ring causes a faster reaction than the corresponding methoxylated compound.

These facts will be discussed in conjunction with possible oxidation mechanisms in the following sections. The reactivity results should also be of use in predicting the ease of peroxyacid oxidation of other aromatic compounds.

HYDROXYLATION

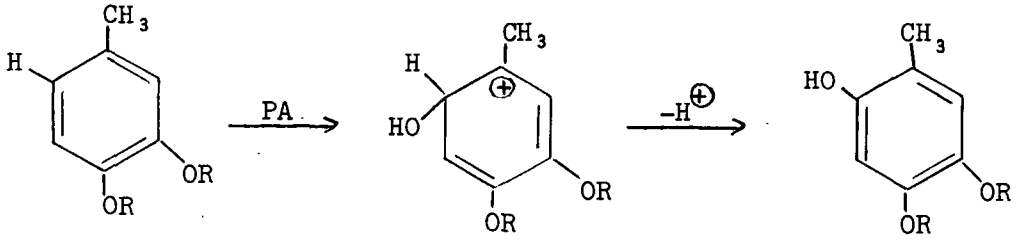
Hydroxylation of an aromatic ring by a peroxyacid could be assumed to proceed by normal electrophilic substitution (5). In p-methylanisole and p-cresol, the most activated positions are ortho and para to the methoxyl or hydroxyl group. The peroxyacid apparently donates a hydroxyl cation $(OH)^+$ in the first step. (Since the p-cresol oxidation is not free radical, as was also indicated for 4-methylpyrocatechol, the oxidation mechanisms must be ionic.) Subsequent electron rearrangement and loss of a proton (or methanol) either restores the aromatic ring or forms the dienone product, depending upon the initial point of attack:



Isolation of 2-hydroxy-p-methylanisole from the p-methylanisole oxidation product is good proof of the initial "ortho" hydroxylation.

p-Methylanisole reacts more slowly than p-cresol as one would expect on the basis of the assumption that electrophilic attack is involved. This is undoubtedly due to the different electron-donating abilities of the two groups: σ_{OH} = -0.37 (para); σ_{OCH_3} = -0.27 (para). Furthermore, the effect of this difference on reactivity is increased as shown in the Hammett equation ($\log k/k_o = \rho\sigma$) by larger rho values (71). (ρ = -4 to -8 for many aromatic substitution reactions.) Also, when two oxygen-containing groups are present, the entire ring would probably be more activated to electrophilic attack.

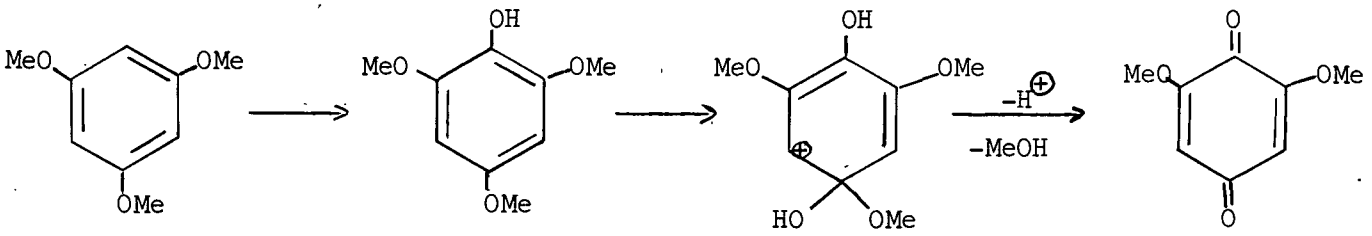
Formation of the 1,2-dioxy intermediate results in activation of a new point on the ring: the C-5 position. Both the C-4 methyl and C-2 hydroxyl or methoxyl activate this position, counteracting the deactivating effect of the C-1 hydroxyl or methoxyl.



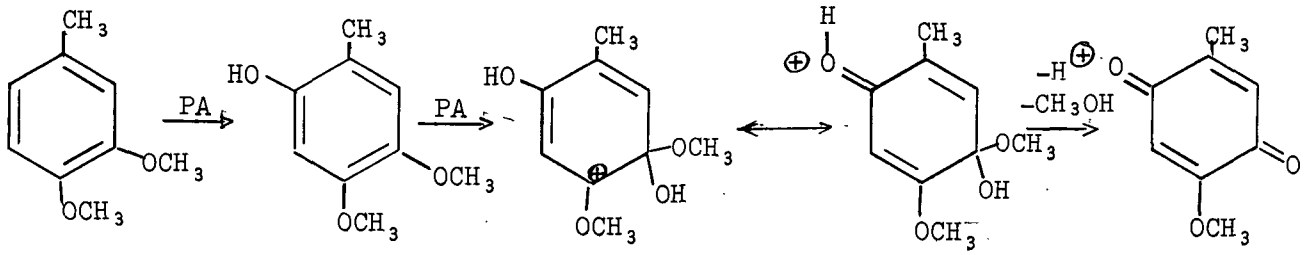
The C-3 position should be activated by the ortho substituents, but no corresponding products were identified, possibly due to steric hindrance.

QUINONE FORMATION

Subsequent oxidation of these 1,2-dioxy and 1,2,5-trioxy intermediates evidently proceeds at positions already substituted by oxygen-containing groups. Friess and coworkers (27) proposed the following mechanism for the oxidation of 1,3,5-trimethoxybenzene to the p-quinone:

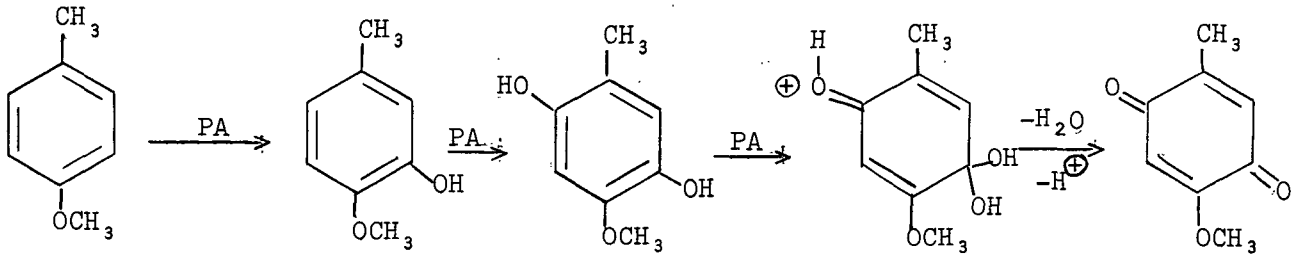


The first hydroxylated intermediate in this sequence is basically the same as the C-5 hydroxy intermediate proposed earlier. Thus, the following similar mechanism can be constructed for 4-methylveratrol:

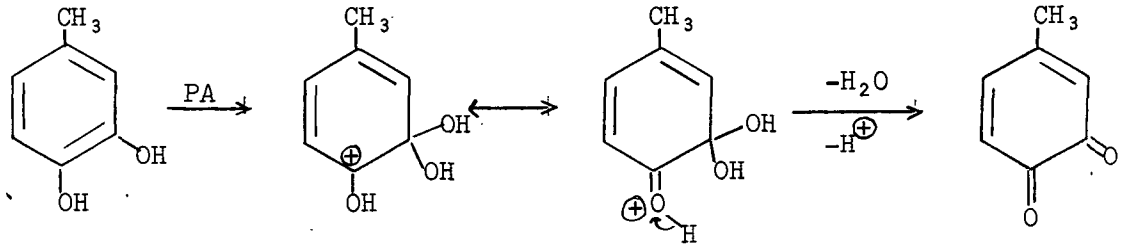


In this mechanism, the peroxyacid deposits the $(OH)^+$ on a site already occupied by a methoxyl group. The newly formed hemiacetal then probably rapidly loses methanol while a proton is released from the para oxygen-containing group.

Since p-methylanisole forms the same p-quinone, a similar oxidation must take place with two hydroxyl groups:

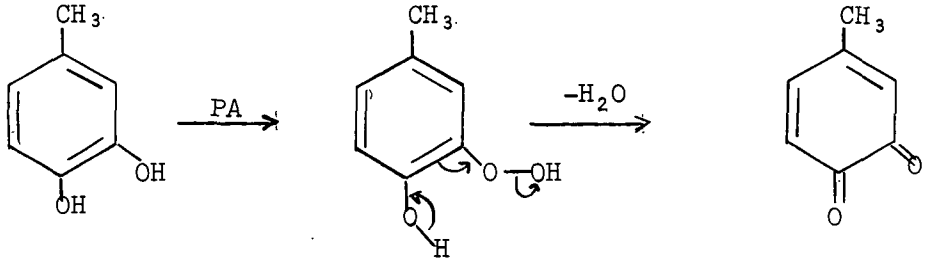


This same mechanism could also be applicable to o-quinone formation:

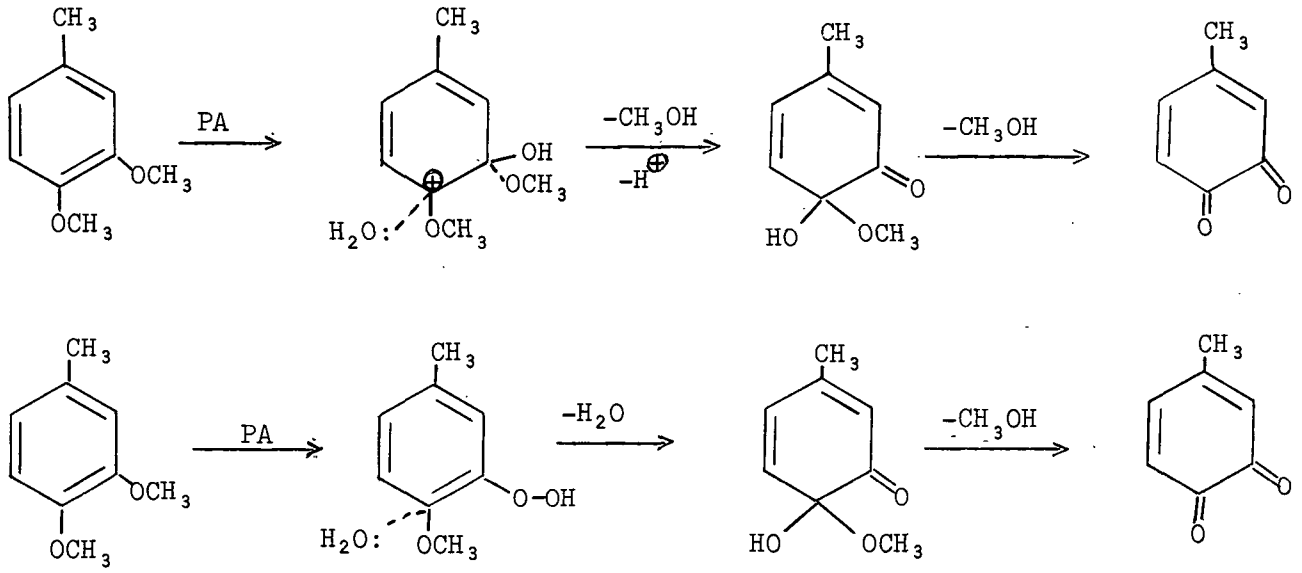


The C-2 gem-diol formed in either of these last two examples would be unstable and rapidly lose water (72). The C-1 or C-5 hydroxyl would lose a proton to give the quinone.

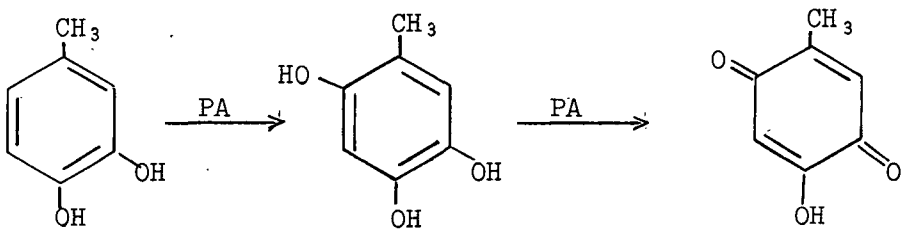
Another possible mechanism could involve direct attack on an oxygen by the peroxyacid to form a hydroperoxide. Although hydroperoxides are not normally found in peroxyacid oxidations, hydrogen peroxide will oxidize secondary and tertiary alcohols to hydroperoxides (7, 73). Thus, the substrate could be oxidized by peroxyacetic acid to an unstable hydroperoxide. The hydroperoxide could then rapidly decompose by loss of water:



Similar reactions could occur with the methoxyl derivatives. However, removal of methyl from both methoxyls may require an additional step:

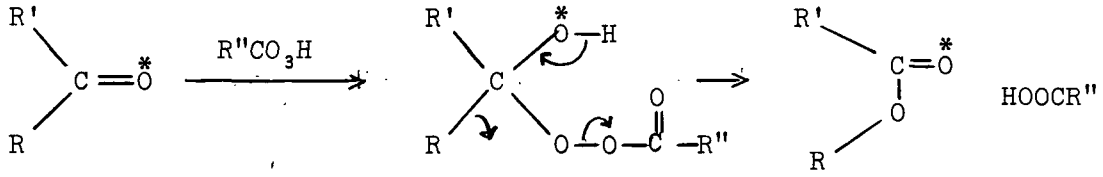


In the peroxyacetic acid oxidation of p-methylanisole and 4-methylveratrole, a 5-hydroxy intermediate has been proposed as leading to the γ-hydroxy-lactone and p-quinone products (p. 75). A similar 5-hydroxy intermediate is apparently formed in the 4-methylpyrocatechol and p-cresol oxidations. It would seem, therefore, that this intermediate could also be oxidized to a p-quinone, in this case, 2-methyl-5-hydroxy-p-benzoquinone. This quinone is stable under dilute acid or base conditions (74).

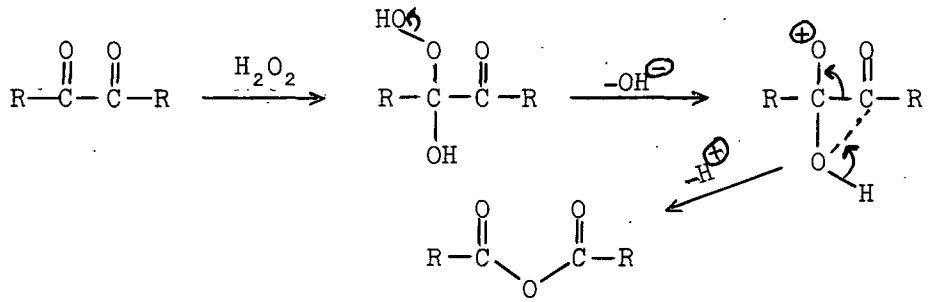


QUINONE OXIDATION

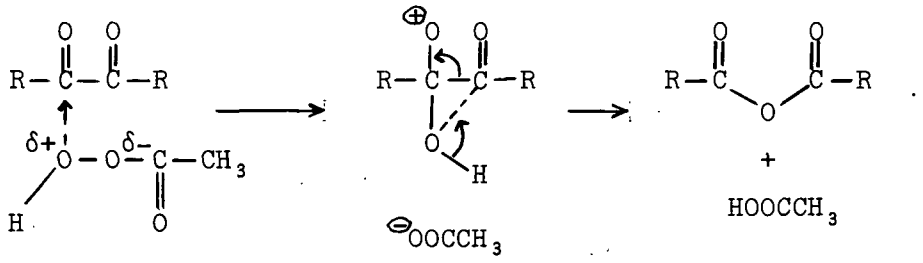
Since an o-quinone is an α-diketo group, its reaction mechanism might be similar to a ketone group. A common mechanism proposed for ketone oxidation involves peroxyacid attack of the carbonyl carbon:



This was proposed by Criegee (16) and is still commonly accepted (75). Retention of the original carbonyl oxygen in the final carbonyl group was supported by tracer studies (75). However, in applying this to the o-quinone oxidation, Leffler (33) noted that α-dicarbonyl compounds always cleave between the two electron-withdrawing carbonyl groups. This is contrary to ketone oxidation results where the group having the most electron-releasing power will migrate (75). Therefore, Leffler proposed the following mechanism for oxidation by hydrogen peroxide:

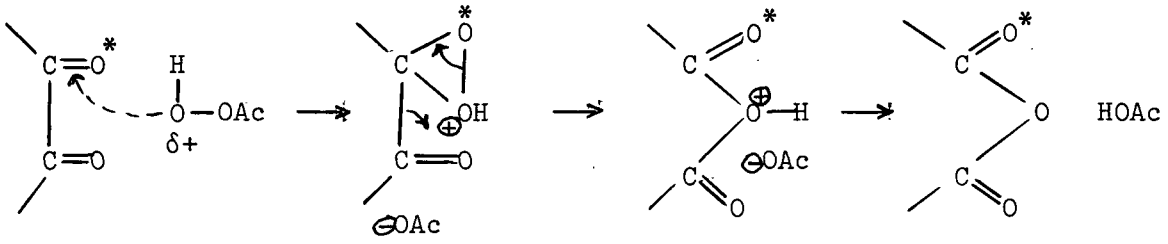


The peroxyacid oxidation could not proceed in exactly this same manner, but the following mechanism would be similar:



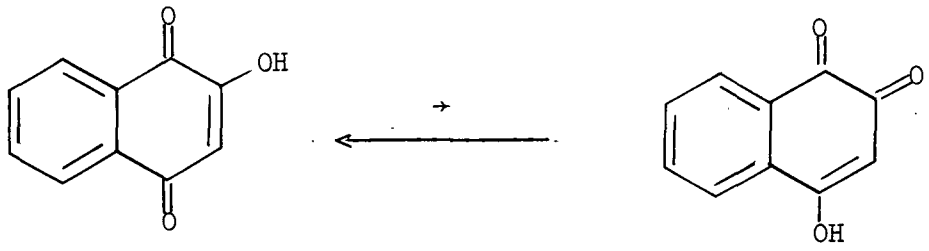
After initial peroxyacid attack on a carbonyl carbon, the remaining electron-deficient carbonyl carbon in the intermediate would seek out the hydroxyl oxygen, with subsequent loss of the hydroxyl proton.

However, the electron-deficient carbonyl carbon would seem to be an unlikely position for initial electrophilic attack. A better possibility might be peroxy-acid attack of the carbon-oxygen double bond. This could rearrange to form a protonated anhydride intermediate and subsequently lose a proton to give the

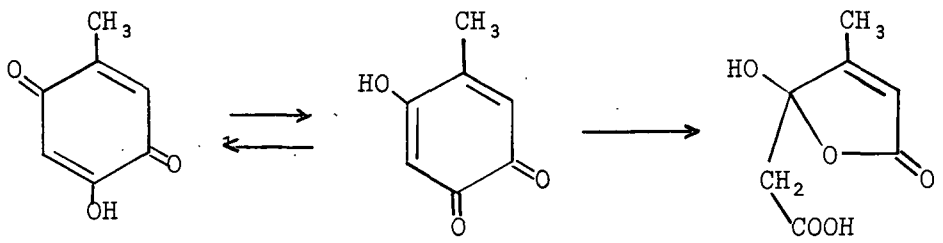


anhydride. If this follows previous ketone oxidations, the original carbonyl oxygen would keep its separate identity throughout the reaction as pictured above. Unfortunately, there is no experimental evidence for any one oxidation mechanism at present.

If the hydroxy-p-quinone proposed earlier did occur, it could possibly exist in two tautomeric forms. 2-Hydroxy-1,4-napthoquinone in solution apparently forms the corresponding o-quinone, although only 0.2% of the latter form is believed to be present (76). Therefore, if the proposed hydroxy-p-quinone intermediate did

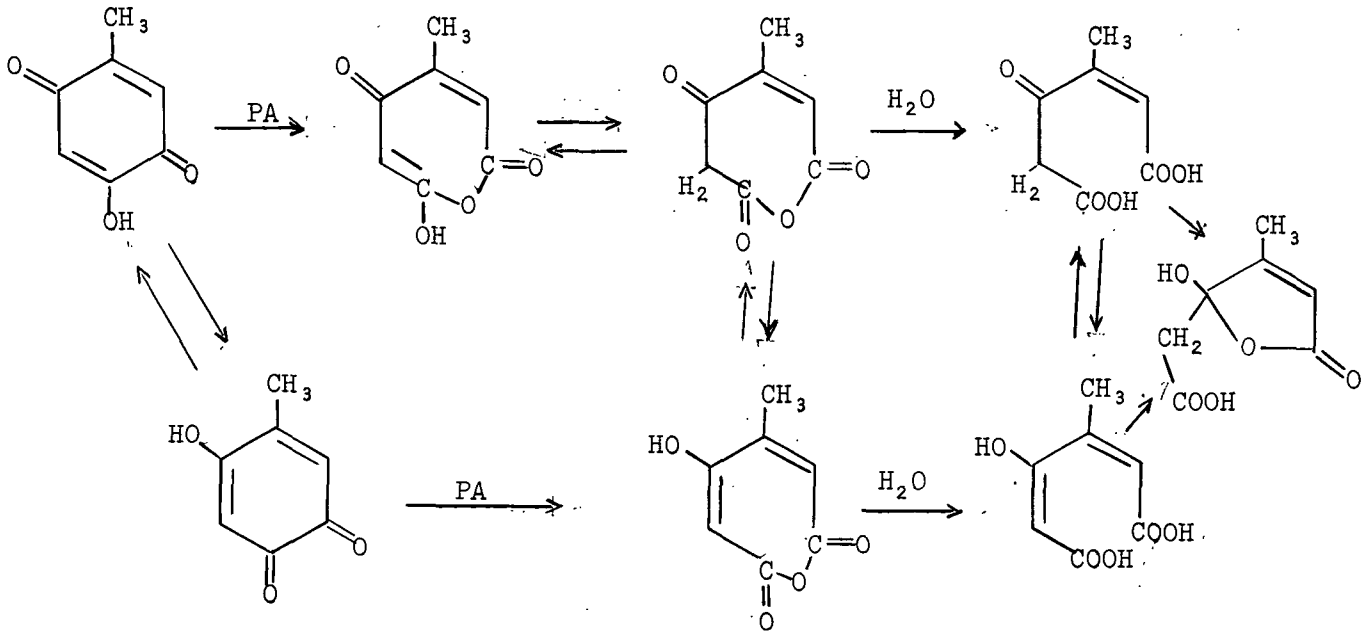


tautomerize to the o-quinone, the latter compound would be consumed immediately by the peroxyacid. Thus, a hydroxy-p-quinone intermediate could indirectly form the



γ-hydroxy-lactone.

However, the hydroxy-p-quinone itself might also be oxidized to a hydroxy-lactone by a Baeyer-Villiger oxidation at the ketone group adjacent to the hydroxyl. Through rearrangement of the initial product, a muconic acid could be formed:



Thus, it would appear that oxidation of a hydroxy-p-quinone, if it were present, would proceed much like the o-quinone. The two quinones and their oxidation intermediates would be merely tautomeric isomers. It is well known that γ-keto acids form stable hydroxy-lactones very readily (55).

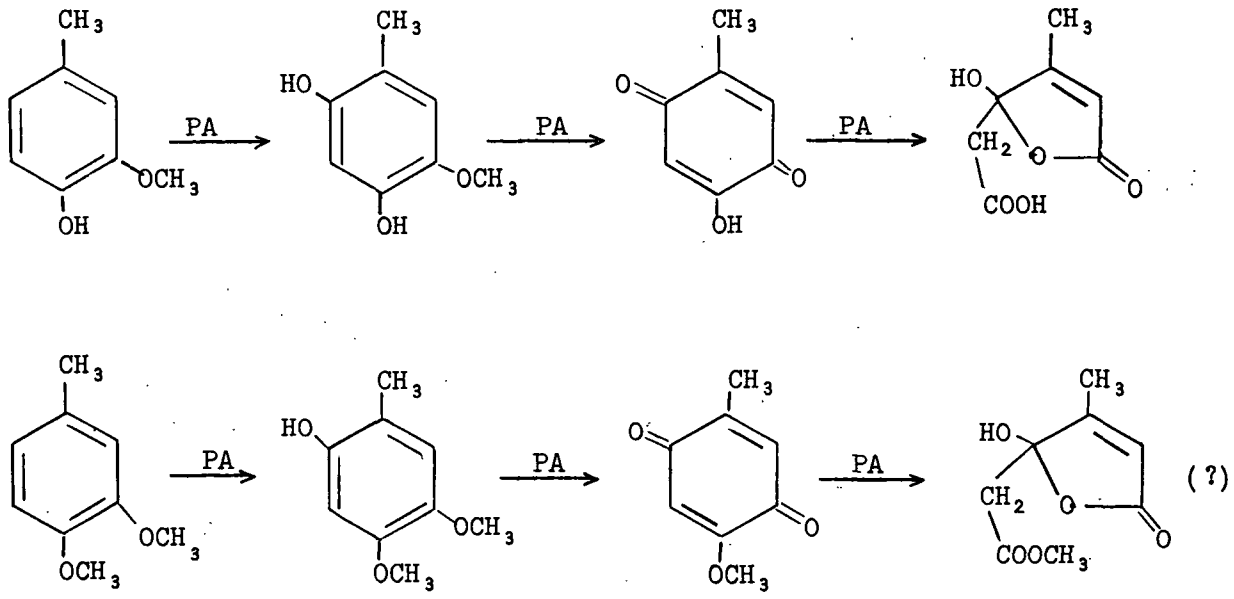
Table XXVII shows the average yields of muconic acids (γ-ML, β-ML, β-MMA, U2, U3, and U4), γ-hydroxy-lactone, volatile products, and the average total yields. The substrates are listed in order of reactivity. It is interesting to note that the three substrates that contain methoxyl groups gave significantly lower yields of muconic acids than the hydroxyl-containing substrates. In the case of p-methylanisole and 4-methylveratrole, this is probably because much of the oxidation is directed toward formation of other products. The oxidation of 2-methoxy-p-cresol gave no noncarboxylic acid products but did form a large amount of γ-hydroxy-lactone.

TABLE XXVII

AVERAGE PRODUCT YIELDS

Substrate	Yield, %			
	Muconic Acids	γ-Hydroxy-Lactone	Neutral Products	Total
4-Methyl-o-quinone	55.4	0	0	55.4
4-Methylcatechol	56.4	5.0	0	61.4
2-Methoxy-p-cresol	19.9	13.4	0	41.4
4-Methylveratrole	13.3	1.2	19.0	33.5
p-Cresol	32.1	4.3	12.7	49.1
p-Methylanisole	14.8	2.0	35.9	52.7

Formation of the p-quinone and γ-hydroxy-lactone products requires prior formation of the 5-hydroxy intermediate. Therefore, since one or the other of these two products was found in good yield from methoxy-containing substrates only, a methoxy group must promote hydroxylation at the C-5 position. At the same time, a methoxyl group apparently slows direct oxidation to the o-quinone intermediate. C-5 Hydroxylation of 2-methoxy-p-cresol would give a hydroxyl para to a methoxyl which would be the same as in the 4-methylveratrole intermediate and thus capable of p-quinone formation. The product data show only that a large amount of the



(?)

5-hydroxy-intermediate is formed; it cannot be said whether oxidation to γ-hydroxy-lactone proceeds preferentially through a hydroxy-o-quinone or through a hydroxy-p-quinone.

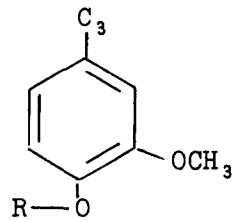
Since the C-5 hydroxy intermediate has been proposed in every oxidation, it would also be possible for a p-quinone to be formed in every oxidation. Thus, oxidation of p-cresol and 4-methylpyrocatechol to γ-hydroxy-lactone can also

apparently proceed via either the hydroxy-p-quinone or hydroxy-o-quinone intermediate as described earlier (p. 81).

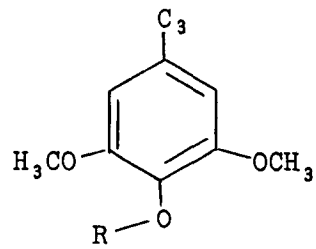
These mechanism discussions clearly show that the substrate oxidations all proceed in much the same way. Therefore, a reaction sequence can be constructed which will account for all of the products that have been formed. This is shown in Fig. 1. The rate of reaction and ratio of products formed are determined by the initial presence and number of hydroxyl or methoxyl groups. This figure shows the formation of muconic acids in every reaction studied. As the overall reactivity of the substrates decreases, the possibility of reactions other than muconic acid formation increases. Thus, the slowest reacting substrate, p-methylanisole, gave the greatest number of products: 4-methyl-o-benzoquinone, the fastest reacting, gave the fewest. This proposed reaction sequence, however, may not account for the undetected products.

APPLICATION TO LIGNIN

Softwood lignins contain polymers of 3-methoxy-4-hydroxy-phenylpropane (guaiacylpropane, XVI). Hardwood lignins contain polymers of 3,5-dimethoxy-4-hydroxy-phenylpropane (syringylpropane, XVII) and 4-hydroxy-phenylpropane in addition to guaiacylpropane (77). Guaiacyl groups having a free phenolic hydroxyl have also been reported in



XVI



XVII

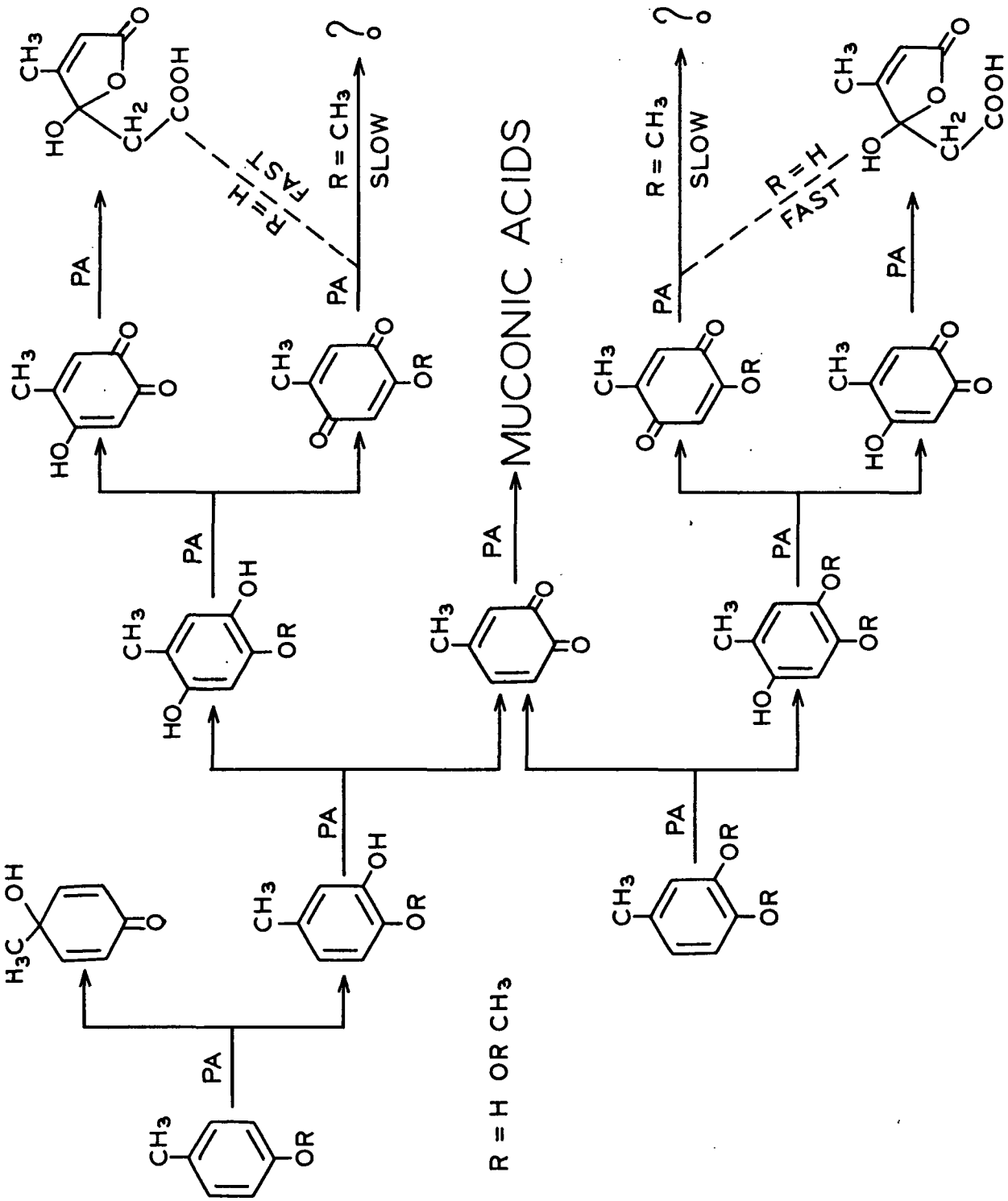
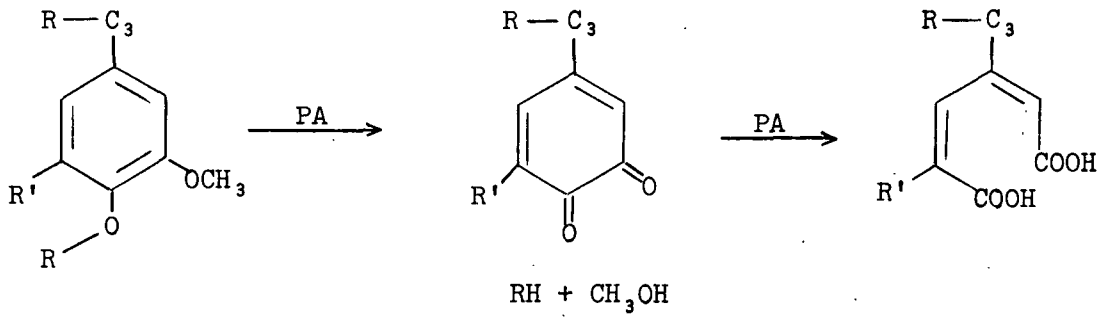


Figure 1. Overall Reaction Scheme

lignin. The main purpose of delignification reactions, therefore is to break up this polymeric network. The fragments can then be washed out of the fibers, removing the main cause of color in paper products.

From what has been found in this thesis, the syringyl structure, having three alkoxy substituents, would probably react faster than other groups when oxidized by peroxyacetic acid. The guaiacyl structure, with one less methoxyl, would probably react to a lesser extent. If these structures were oxidized to muconic acid derivatives, an o-quinone intermediate would cause cleavage of the polymer at that point:



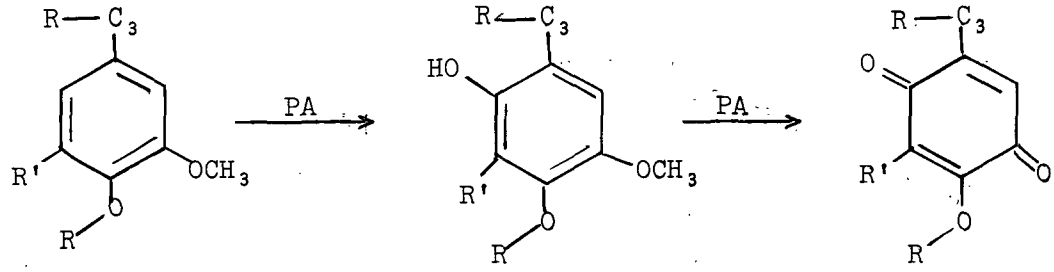
RH + CH_3OH

R = adjacent lignin polymer unit

The effect of the "R" group on this oxidation is unknown. However, destruction of aromatic rings and formation of muconic acids has been reported in the literature for peroxyacetic acid pulping reactions (42-44).

A guaiacyl group with a free phenolic hydroxyl in lignin would also be very reactive. But this reaction would not help break up the lignin polymer since this would not be a branch point. However, it may increase lignin solubility in water by formation of carboxyl groups.

It would also seem that oxidation to a p-quinone could occur. This, however, would serve no practical purpose in aiding delignification and would only cause



coloration of the pulp if not washed out.

This has been a brief and simplified description of how peroxyacetic acid might be expected to oxidize aromatic rings in lignin, based on the results of this thesis. There are, however, other reactions that could take place at the olefin and carbonyl groups on the side chains. These groups would be expected to react with peroxyacetic acid, as described in the introduction. Thus, lignin could be oxidized by peroxyacetic acid in several different ways.

EXPERIMENTAL PROCEDURES

PREPARATION OF COMPOUNDS

COMMERCIAL CHEMICALS

The following reagents used in the peroxyacetic acid oxidations were obtained from K & K Laboratories, Inc.: p-methylanisole, p-cresol, 4-methylpyrocatechol, and 4-methylveratrole. Mesitylene was obtained from Aldrich Chemical Company. The purity of each reagent was checked by gas-liquid chromatography (GLC), and all contained less than 1% impurity. However, 2-methoxy-p-cresol, obtained from Eastman Chemicals, contained about 5% impurity. (This was not 4-methylpyrocatechol as might be expected.)

The purity of the internal standards was not examined quantitatively. However, injection of each internal standard in sufficient quantity to give a full-scale peak gave no evidence for any impurity.

4-METHYL-o-BENZOQUINONE

This compound was prepared by the method of Horner and Burger (78). A solution of 10 g. (39 mmole) of tetrachloro-o-benzoquinone in 100 ml. abs. ether was added to a second solution of 4.5 g. 4-methylpyrocatechol in 5 ml. abs. ether. After mixing, the solution immediately turned from red-orange to a very deep red and was then placed in a freezer for three hours. By the end of this time, red 4-methyl-o-benzoquinone precipitated out of solution. The precipitate was filtered out with the exclusion of moisture and washed with 100 ml. of abs. ether cooled to -15°. The washed precipitate was allowed to dry overnight in a desiccator over phosphorous pentoxide at ∿ 25 mm. Hg. The next day the o-quinone was weighed (2.1 g., 47%) and used within a few hours. NMR analysis confirmed the o-quinone structure but also showed the

presence of a significant amount of some impurity. This impurity was not 4-methylcatechol as might have been expected.

γ-CARBOXYMETHYL-β-METHYL-$\Delta^{\alpha,\beta}$-BUTYROLACTONE

The method of Pauly, Gilmour, and Will (79) was used to prepare this lactone. Concentrated sulfuric acid (600 g.) was heated to 110-115° in a 1000-ml. flask with constant stirring. 2-Nitro-p-cresol (warmed to keep it liquid) was transferred slowly to the flask containing sulfuric acid while closely monitoring the temperature to hold it at 115-120°. All of the 2-nitro-p-cresol was added within two hours, after which the black solution was allowed to cool to room temperature and then poured over crushed ice. The solution then was mixed with Norit A (activated charcoal) and filtered. This decoloration step was repeated several times. The final clear orange solution was continuously extracted by ether for six days. The extracted product was recrystallized from water and finally from 1:3 ethanol/benzene. The final isolated crystals were colorless with a melting point 126.2-128.0° [lit. m.p. 130° (79)]. NMR and infrared analyses confirmed this structure.

PEROXYACETIC ACID

Peroxyacetic acid was prepared by the hydrogen peroxide oxidation of acetic acid with sulfuric acid as catalyst, using the method described by FMC (80).

$$CH_3COOH + H_2O_2 \xrightarrow{H_2SO_4} CH_3CO_2OH + H_2O$$

A description of the peroxyacetic acid generator apparatus is shown in Fig. 2 and the legend in Table XXVIII. The entire apparatus was passivated the first time it was used by the procedure described in the next section. Since the generator was used every three or four months, it was not passivated again but simply rinsed with distilled water before each use.

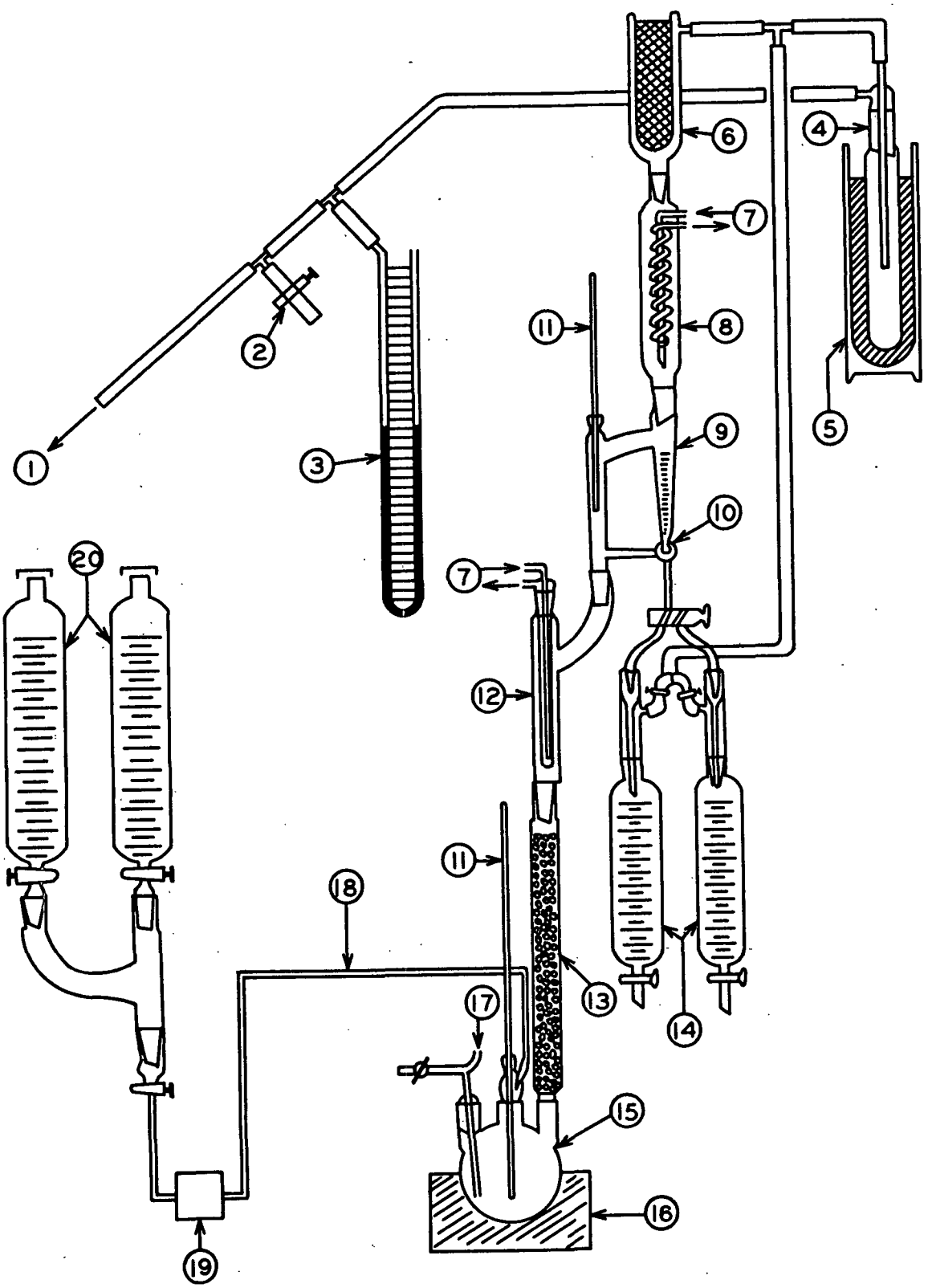


Figure 2. Peroxyacetic Acid Generator According to FMC Corporation (80)

TABLE XXVIII

APPARATUS LEGEND FOR PEROXYACETIC ACID GENERATOR

1. Vacuum pump
2. Tubing clamp: vacuum release
3. Manometer
4. Vacuum trap: two piece
5. Dewar flask filled with ice-salt mixture
6. Dewar condenser filled with ice-salt mixture
7. Cooling water
8. Condenser coil
9. Modified Dean-Stark trap
10. Three-way stopcock
11. Thermometer
12. Modified Hopkins finger condenser
13. Distilling column, 37 mm.: 1/4-in. glass helices packing
14. 500-ml. cylindrical separator funnels (receiving)
15. 1000-ml. three-neck flask
16. Constant temperature water bath
17. Emergency water flood
18. 1/8-in. Tygon tubing: feed line
19. Sigma pump
20. 1000-ml. separatory funnels (feed)

The make-up of the solutions used in the generator is shown in Table XXIX. The premix was placed in the reaction flask (15) and the feed solution in the feed cylinders (20). The water bath was heated to 65-66°, giving a flask temperature of 50-51° at 60 mm. Hg. The solution was refluxed until the system had come to equilibrium. Then the three-way valve (10) was turned to allow transfer of the distillate to the receiving flasks. The flow rate of the finger condenser (12) cooling water was adjusted to give a distilling rate of 1.5-2.5 ml./min. The composition of the final peracid solution was generally about 35% peroxyacetic acid, with about 0.1% hydrogen peroxide, 5% acetic acid, and 60% water (81). The generator peroxyacetic acid solutions were stored at 5°.

TABLE XXIX

GENERATOR SOLUTIONS

	Premix Solution, g.	Feed Solution, g.
Distilled water	114	590
Concd. sulfuric acid	115	--
Glacial acetic acid	51	440
50% Hydrogen peroxide	270	470
Dipicolinic acid	0.28	--

PASSIVATION OF GLASSWARE

Since peroxyacetic acid is subject to catalytic decomposition by traces of metal ions, it was important that all reaction vessels be as free as possible from metal contaminants. The following passivation procedure (80) was used to accomplish this.

1. Degreasing with alkaline detergent — Alconox
2. Distilled water wash
3. 15-Minute soak in 0.5% sodium hydroxide
4. Distilled water wash
5. 45-Minute soak in 35% nitric acid
6. Distilled water wash
7. Overnight soak in 30% hydrogen peroxide
8. Distilled water wash

This procedure was carried out from time to time during the course of the study and especially before important oxidations such as the kinetic runs. After every use, each flask was washed with distilled water, acetone, methanol, and a final rinse in absolute ethanol. The clean flask was sealed with parafilm (Marathon) when not in use.

PROCEDURES FOR PRODUCT ANALYSIS

REACTION CONDITIONS

Prior to each oxidation, the generator peroxyacetic acid solution was diluted to $\sim$ 10% by glacial acetic acid. Thus, a generator solution, originally 35% in peroxyacetic acid, after dilution would be 10% peroxyacid, 73% acetic acid, 17% water, and < 0.1% hydrogen peroxide. However, as the peroxyacid spontaneously decomposed, the acetic acid and hydrogen peroxide content increased, which could cause a change in the oxidizing characteristics of the peroxyacid solution. For this reason,

oxidations were run as soon as possible after fresh peroxyacetic acid was made (usually within two weeks). Over a two-week period, the original peroxyacetic acid solution would decompose from 35% peroxyacid and 0.1% hydrogen peroxide to about 32% peroxyacid and 1.0% hydrogen peroxide. Thus, after diluting to 10% peroxyacetic acid, these solutions would contain from 0.04 to 0.3% hydrogen peroxide.

All oxidations were run in passivated 50-ml. round bottom flasks. About 12 mmoles of substrate was weighed into a flask and 25.0 ml. (∿ 27 g., 36 mmole) of the ∿ 10% peroxyacetic acid solution added. The flasks were then placed in a constant temperature bath at 25°. However, oxidations involving 4-methylcatechol and 4-methyl-o-benzoquinone had to be cooled under cold tap water to slow the rapid initial reaction. After this initial period, these flasks were also placed in the constant temperature bath. The flasks were closed with a ground-glass stopper. No attempt was made to eliminate air, although the oxidations were run in darkness.

PEROXYACETIC ACID AND HYDROGEN PEROXIDE ANALYSIS

There are two methods commonly used in the titration of peroxyacid solutions, both based on the potassium iodide reduction of the peroxyacid. The method of Ledaal and Bernatek (82) involved the potassium iodide reduction of the peroxyacid but also complexed any hydrogen peroxide present with titanic sulfate, which was later broken down and analyzed. This is an accurate method since there is one end point for the peroxyacid titration and a second for the release of hydrogen peroxide. However, this procedure is somewhat involved, and a complete analysis of one sample would require over one hour.

The method of Sully and Williams (83) was used in this thesis. It is a simple procedure, and the analysis time is generally less than ten minutes. Peroxyacetic

acid and hydrogen peroxide are determined in the presence of each other by taking advantage of the large difference in their rates of reaction with iodide ion. The rate of equilibration between peroxyacetic acid and hydrogen peroxide is negligible in the 3-5 pH range used. The exact procedure as outlined by Sully and Williams was as follows:

1. Acetic acid, 0.1N (100 ml.), was placed in a 500-ml. Erlenmeyer flask and cooled to about 5° in an ice bath.

2. A weighed sample ($\leq$ 1 g.) of the peroxyacid solution was transferred to this flask and allowed to mix a few minutes.

3. Then 10 ml. of 15% potassium iodide was added and a stopwatch started at the same moment.

4. This final solution was immediately titrated by 0.100N sodium thiosulfate with starch indicator.

5. The first end point was passed by one drop, and the instant of color return was noted on the stopwatch and recorded along with the amount of thiosulfate used (t_1, x_1).

6. The overtitration was repeated once more on the same sample and the second end point noted (t_2, x_2). These two end points were generally about two minutes apart due to the slow reaction of hydrogen peroxide with potassium iodide.

7. Finally, about 10 drops of ammonium molybdate solution was added to catalyze the reduction of hydrogen peroxide by potassium iodide.

8. The sample was titrated until the solution remained colorless for at least one minute (x_t).

The concentration of peroxyacetic acid and hydrogen peroxide was calculated using the following equations.

$$x_0 = x_1 - \frac{t_1(x_2-x_1)}{t_2-t_1}$$

$$\text{Peroxyacetic Acid, \%} = x_0(0.3803)/w$$

$$\text{Hydrogen Peroxide, \%} = (x_t-x_0)(0.1701)/w$$

where

x_1 = ml. thio at first end point,

t_1 = time elapsed to first end point,

x_2 = ml. thio at second end point,

t_2 = time elapsed to second end point,

x_t = ml. thio at final end point, and

w = weight of sample, g.

The ammonium molybdate catalyst was prepared as follows:

> 100 g. of molybdic anhydride was dissolved in a mixture of 400 ml. of water and 80 ml. of ammonia solution (sp. gr. 0.880). This solution was added slowly, with stirring, to a mixture of 400 ml. concentrated nitric acid and 600 ml. of water. The product was stored in a warm place for several days and any sediment was removed by decantation.

This titration method, besides having a short analysis time, gave very consistent results with a precision range of $\pm$ 0.1% to $\pm$ 1% for peroxyacid concentrations from 10 to 1%, respectively.

In the analysis of freshly prepared peroxyacid solutions, a slight variation in the procedure was made. The low hydrogen peroxide content caused an extremely slow formation of color after the first end point so that cooling in an ice bath resulted in a long time between the first two titrations. To speed this up, the ice bath was not used, and fresh peracid solutions were titrated at room temperature.

PRODUCT WORK-UP

At the desired time, the oxidation solution was removed from the constant temperature bath. If a stoichiometry analysis was to be carried out on the product, one or two 1.0-ml. aliquots were withdrawn and titrated as described in the previous section. Following this, the remaining product solution was mixed with 15 ml. of

acetaldehyde or 4 g. of sodium bisulfite to reduce the peroxyacetic acid remaining. The advantage of using acetaldehyde was that acetic acid was supposed to be the only final product of this reaction (84, 85) and thus, no new materials would be added to the system. Unfortunately, it was later discovered that other very volatile products were formed; they were neglected in chromatograms of product mixtures.

If a product analysis was to be carried out, the entire product solution was reduced by 15 ml. of acetaldehyde. Sodium bisulfite was used only in those oxidation products on which no product analyses were to be performed. It was found that reduction by bisulfite caused the disappearance of several carbonyl-containing products, probably a result of formation of the bisulfite adduct. Acetaldehyde reduced all of the peroxyacid within 20 minutes while sodium bisulfite gave complete reduction within ten minutes and for this reason was used for stoichiometry determinations. Neither compound, however, had any effect on the hydrogen peroxide present.

About an hour after the product solution had been reduced, it was transferred to a 250-ml. Erlenmeyer flask and mixed with sodium carbonate, neutralizing the acetic acid and any other carboxylic acids present. It was found that at times some of the p-quinone present in the product was decomposed during this step, probably due to oxidation by oxygen. Therefore, a slow stream of nitrogen was used to flush other gases out of the flask during neutralization in later work-ups. This alkaline solution (pH 8) was then extracted by ethyl ether to remove all noncarboxylic organics (neutral products) and the ether extract was dried over anhydrous magnesium sulfate.

The remaining alkaline layer from this extraction was acidified to about pH 2 (congo red) by slowly adding concentrated hydrochloric acid. The acidified alkaline extract was then concentrated *in vacuo* at about 50° to remove the acetic acid. After concentration to dryness, the resulting material was diluted with water and concentrated again to dryness to remove as much acetic acid as possible. Often a

small amount of black, tarlike material was formed during this step, but usually the final concentrate was just a light brown-colored solid.

The final concentrate was diluted once more in a minimum amount of water and transferred to a continuous extractor to be extracted by ether for 24 hours. At the end of this time, the ether extract of the original alkaline layer was removed and dried over anhydrous magnesium sulfate. This final ether extract contained the carboxylic acid products.

However, in a few 4-methylpyrocatechol oxidations, the product was not worked-up as above, but simply concentrated in vacuo (50°). The concentrate was diluted again with water and concentrated to a sirup. This final concentrate was dissolved in ether and dried over magnesium sulfate to give the carboxylic acid products ready for further analysis. Since no transfers or extractions were involved in this preparation, there was no opportunity to lose any product.

A final 4-methylpyrocatechol oxidation product was prepared for analysis by diluting the reduced product with water after the product solution had been reduced and freeze-dried. The product was diluted with water once more and again freeze-dried to remove as much acetic acid as possible. This final concentrate was then diluted in ether and dried over magnesium sulfate. Since no heat was involved in the concentration step, this was a milder preparation than the previous one.

GAS CHROMATOGRAPHY

Two different gas chromatographs were used in this study, both made by Varian-Aerograph with thermal conductivity detectors. A model A90-S unit, used in earlier work, was later replaced by a Moduline 202-C dual column gas chromatograph equipped with a linear temperature programmer. All response factors were determined again when the new instrument was received. A Sargent Model S recorder was used.

Qualitative and Quantitative GLC

Neutral Products (Ether Extract)

The original ether extract of each product contained nonacidic organic compounds which were volatile enough for analysis by gas-liquid chromatography (GLC) without further treatment. The ether extract was transferred to a 250-ml. round bottom flask and concentrated in vacuo and transferred to a 50-ml. round bottom flask for final concentration to ∿ 10 ml.

A different concentration method was used in some p-methylanisole oxidations (No. 2601-117-1, -2, -3, -4, 2601-157-2). Since p-methylanisole is relatively volatile, the ether extract was distilled from a 250-ml. round bottom flask through a straight 8-inch column to remove the ether without losing any p-methylanisole.

The final concentrate of the ether extract was then injected on a Carbowax 20M column at 120 ml./min. helium flow rate, with the temperature programmed from 100° to 160° at 2°/min., giving the entire spectrum of products.

Quantitative analysis of all products and remaining starting materials involved internal standardization (86). This method involves the use of an appropriate material as internal standard and determination of the response factor for the material to be analyzed. The response factor can be determined by injecting a known mixture of the internal standard and the substrate of interest into the gas chromatograph and using the following equation in calculating the results:

$$F = (A_r/A_s)(W_s/W_r)$$

where

F = response factor,

A_r = area of reference (internal standard),

A_s = area of substrate,

W_r = weight of reference present, and

W_s = weight of substrate present.

A known amount of the internal standard is added to the entire product solution, samples injected in the gas chromatograph, and the resulting peak areas determined. Earlier peak areas were found by triangulation (86) but most were determined by a Technicon Model AAG Integrator/Calculator. Both of these methods gave results with an average deviation of about 3%. As long as peaks are symmetrical, the integration method will be only slightly more accurate. However, if the peak is skewed in any way, triangulation will not give a true figure for peak area and an integrator must be used. In this study, triangulation was used in the earlier stoichiometry analyses while most of the product analyses results were determined with the integrator. The results were then used in the following equation to find the weight of substrate present:

$$W_s = W_r(A_s/A_r)F$$

Some difficulty was encountered with the quantitative GLC of 2-methyl-5-methoxy-p-benzoquinone; it seemed to be sorbing more and more with use on the Carbowax 20M column. Finally it was found that an SE-30 column (125°, 75 ml. He/min.) gave a more symmetrical peak with good reproducibility and little tailing.

Carboxylic Acid Products

Products found from the alkaline extracts were analyzed as described in the preceding section with the exception that they first required treatment to make them volatile enough for GLC analysis. Therefore, the final ether solution of the alkaline extract products (carboxylic acids) was filtered and concentrated *in vacuo* to minimum volume, generally leaving a yellow sirup still containing a small amount of acetic acid.

Methylation procedure. Originally, these products were then methylated by dissolving the sirup in a 10% hydrogen chloride/methanol solution. The HCl/methanol solution was made by carefully adding acetyl chloride to methanol. After 24 hours reaction, the methanol solution was diluted with water, neutralized by sodium bicarbonate, and extracted with ether to remove the newly formed methyl esters. GLC analysis of these methyl esters gave a qualitative description of the relative amounts of carboxylic acid products.

Silylation procedure. Subsequent qualitative and quantitative analyses of these products were carried out by forming the trimethylsilyl esters. Bis(trimethylsilyl)trifluoroacetamide (trade name Regisil, Regis Chemical Co.) was used as the silylating agent in the following manner (57):

1. The ether solution of the alkaline extract product was filtered and concentrated in vacuo in a tared 50-ml. round bottom flask, leaving ∿ 5 ml. of solution. This was injected on Carbowax 20M (165°, 120 ml./min.) to find if any ether extract products were present.

2. When ether extract products were found, a small amount of 1,2,4-trimethoxybenzene (0.1 g.) was added to the product solution and again chromatographed. However, in only one product was a significant amount of product found (dienone). Using a response factor of 1.0, the approximate amount present was calculated and added to the previously determined figure.

3. Following this, the entire product was concentrated to dryness or minimum volume under high vacuum at 50° and reweighed to determine the total weight of material present.

4. The product was then dissolved in acetone and transferred to a 100-ml. volumetric flask and diluted to the mark.

5. A portion of this solution was removed, placed in a 50-ml. R. B. flask and concentrated to dryness.

6. The concentrate was dissolved in dimethylformamide (1/2-1 ml.) and treated with Regisil in the ratio 2 μl./mg. product.

7. After reacting 30 minutes, this solution was chromatographed on SE-30 (165°, 75 ml./min.).

8. Next adipic acid (internal standard) was added to this solution along with more Regisil. Further additions of Regisil were made until no change took place in succeeding chromatograms. Regisil and its reaction product did not interfere with other peaks.

9. The resulting peak areas were then determined using the Technicon Integrator.

Preparative Gas Chromatography

Since most of the products encountered in this study were unknown, it was necessary to collect them for subsequent infrared and NMR analysis. In most cases, a preparative carbowax 20M column (3/8 in. x 6 ft.) was used to collect the products. A 6-inch piece of 3-4 mm. glass tubing, bent at a right angle in the middle, was inserted in the exit port at the proper time. A piece of dry ice was held against the elbow of the tubing to condense as much product as possible. Generally, 2-12 mg. of material were collected depending on peak size. GLC conditions and product retention times are shown in Table II (p. 17) and Appendix V.

ANALYSIS OF PRODUCTS

Every major product of the oxidation was collected in addition to several minor ones. Many products were common to all substrate oxidations and were rigorously identified (IR, NMR, mass spectrum). Where these products were also apparently present in other substrate oxidations, they were collected in small quantities and the infrareds simply compared to those previously identified. Thus, a definite identification was made of every major product and some minor ones from all four main substrate oxidations.

Samples collected in glass tubing as above were flushed out of the tubing by a suitable deuterated NMR solvent and examined by NMR in a microtube (150 µl.). A Varian A60A instrument was used for analysis. After NMR analysis, the solution was evaporated and the residue examined by infrared on a Perkin Elmer Model 21 sodium

chloride prism infrared spectrophotometer or a Perkin Elmer Model 621 grating infrared spectrophotometer. Often a very small amount of material was collected so that only a microinfrared analysis could be carried out. Solids were analyzed by preparing the sample in potassium bromide micropellets. Small liquid samples were examined by either placing them between two blank KBr pellets or by spreading the liquid on the surface of a blank micropellet. Larger liquid samples were examined between sodium chloride plates.

Mass spectral analyses were performed by Morgan Schafer Corporation (Canada) on a Hitachi RMU-6D instrument.

WORK-UP CONTROLS

Because of the many stages in the work-up procedure where material could conceivably be lost, it was necessary to run known materials through various parts of the work-up. All of the starting materials and several oxidation products were run through the complete work-up procedure. It was found that a considerable amount of p-methylanisole was lost in work-ups involving the use of a nitrogen stream and concentration in vacuo (Table LVI). Therefore, it was necessary to correct the results of those reactions that were worked-up in this manner. The corrections made are listed in Table LV in Appendix VI.

In a similar manner, the stability and work-up yield of the major products was also checked. 2-Methyl-5-methoxy-p-benzoquinone, cis, trans-β-methylmuconic acid and β-methyl-γ-carboxymethyl-$\Delta^{\alpha,\beta}$-butyrolactone (β-methyl-lactone) were all dissolved in peroxyacetic acid solutions (4-8%) and worked-up after sufficient reaction time. The decomposition of peroxyacetic acid was followed in the β-methyl-lactone, and p-quinone oxidations, and the stoichiometry determined for the

latter compound. The stability of the methyl ester of this β-methyl-lactone was also studied. The β-methyl-lactone and p-quinone were then run through the standard work-up procedure, and the yields were determined.

STOICHIOMETRY DETERMINATIONS

Each time a reaction was run for the purpose of determining its stoichiometry, a blank was also run containing the peroxyacetic acid solution only. Titration of the blank at the end of the oxidation gave the amount of spontaneous decomposition of peroxyacid. This blank was then used as a correction for the peroxyacetic acid decomposition in the oxidation solution.

The results from the GLC analysis of the remaining substrate had to be corrected for the aliquots withdrawn for peroxyacid titration in order to obtain the true figure for the amount of substrate remaining. The stoichiometry was then determined by calculating the ratio of mmoles peroxyacetic acid consumed to the mmoles of substrate reacted. A sample stoichiometry calculation is shown in Table LIII in Appendix VI.

EFFECT OF METHYL METHACRYLATE

The oxidation of p-cresol by peroxyacetic acid was studied further in an effort to determine whether free radicals were formed during the reaction. Methyl methacrylate, an excellent free-radical scavenger, was mixed (3.3%) in a p-cresol oxidation mixture made up exactly as described earlier. The decomposition of peroxyacetic acid was followed by titration over a period of time and compared to a simultaneous p-cresol oxidation that contained no methyl methacrylate but was otherwise identical. Another p-cresol oxidation was run in the presence of methyl methacrylate, worked up at the end of the reaction, and a complete product analysis was carried out.

CONCLUSIONS

p-Cresol and p-methylanisole are initially hydroxylated ortho and para to the original oxygen-containing group, analogous to electrophilic aromatic substitution. Para-hydroxylation gives a hydroxy-cyclohexadienone product, while ortho-hydroxylation results in the "1,2-dioxy" intermediate. Subsequent oxidation of "1,2-dioxy" compounds involves either direct oxidation to an o-quinone intermediate or further hydroxylation at the C-5 ring position. The o-quinone is rapidly oxidized to an anhydride, which opens in water to form the muconic acid products. Direct formation of the o-quinone is evidently inhibited by methoxyl groups at the C-1 and/or C-2 positions, while C-5 hydroxylation is favored.

The "1,2,5-trioxy" intermediate is then oxidized either to a hydroxy-o-quinone or to a methoxy-p-quinone. Formation of a hydroxy-p-quinone is also possible. The hydroxy-o-quinone and hydroxy-p-quinone are oxidized finally to γ-hydroxy-β-methylmuconic acid, which is isolated as a hydroxylactone. The methoxy-p-quinone product reacts slowly in the oxidizing solution to form an unknown product or products. Other unknown oxidations occur when the C-2 group is a methoxyl.

The higher reactivity of 1,2-dioxy substrates and hydroxyl groups in general is apparently due to greater activation of the ring. The presence and number of hydroxyl or methoxyl groups also controls the stability and relative yields of products.

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LITERATURE CITED

1. Waters, W. A. Oxidation processes. In Gilman's Organic chemistry. Vol. 4. p. 1154-73. New York, John Wiley and Sons, Inc., 1953.

2. Giguere, P. A., and Olmos, A. W., Can. J. Chem. 30:821-30(1952).

3. Brooks, W. V. F., and Haas, C. M., J. Phys. Chem. 71:650-5(1967).

4. Morrison, R. T., and Boyd, R. N. Organic chemistry. p. 284-301. Boston, Allyn and Bacon, Inc., 1959.

5. Gould, E. S. Mechanism and structure in organic chemistry. p. 412-52. New York, Holt, Rinehart, and Winston, 1959.

6. Koubek, E., Haggett, M. L., Battaglia, C. J., Ibne-Rasa, K. M., Pyun, H. Y., and Edwards, J. O., J. Am. Chem. Soc. 85:2263-8(1963).

7. Wallace, J. G. Hydrogen peroxide in organic chemistry. E. I. duPont de Nemours & Co. 142 p.

8. FMC Corporation. Preparation, properties, reactions, and uses of organic peracids and their salts. New York, 1964.

9. Swern, D., Chem. Rev. 45:1-68(1949).

10. Swern, D., J. Am. Chem. Soc. 69:1692-8(1947).

11. Swern, D. Epoxidation and hydroxylation of ethylenic compounds with organic peracids. In Adam's Organic reactions. Vol. 7. p. 378-433. New York, John Wiley & Sons, Inc., 1953.

12. Hassall, L. H. The Baeyer-Villiger oxidation of aldehydes and ketones. In Adam's Organic reactions. Vol. 9. p. 73-106. New York, John Wiley & Sons, Inc., 1957.

13. Baeyer, A., and Villiger, V., Ber. 32:3625-33(1899).

14. Friess, S. L., J. Am. Chem. Soc. 71:14-15(1949).

15. Friess, S. L., and Farnham, N., J. Am. Chem. Soc. 72:5518-21(1950).

16. Criegee, R., Ann. 560:127-35(1948).

17. Mateos, J. L., and Menchaca, H., J. Org. Chem. 29:2026-8(1964).

18. Wenkert, E., and Rubin, M., Nature 170:708-9(1952).

19. Elvidge, J. A., Linstead, R. P., and Sims, P., J. Chem. Soc. 1951:3398-402.

20. Karrer, P., Schwyzer, R., and Neuwirth, A., Helv. Chim. Acta 31:1210-14(1948).

21. Chambers, R. D., Goggin, P., and Musgrave, W. K. R., J. Chem. Soc. 1959:1804-7.

22. Boeseken, J., Metz, C. F., and Pluim, J., Rec. Trav. Chim. 54:345-52(1935).

23. Wacek, A., and Fiedler, R., Monatsh. Chem. 80:170-86(1949).

24. Grundman, C., and Trischmann, H., Ber. 69B:1755-7(1936).

25. Elvidge, J. A., Linstead, R. P., and Sims, P., J. Chem. Soc. 1951:3386-98.

26. Bryce-Smith, D., and Gilbert, A., J. Chem. Soc. 1964:873.

27. Friess, S. L., Soloway, A. H., Morse, B. K., and Ingersoll, W. C., J. Am. Chem. Soc. 74:1305-9(1952).

28. Davidge, H., Davies, A. G., Kenyon, J., and Mason, R. F., J. Chem. Soc. 1958:4569-73.

29. Fernholz, H., Ang. Chem. A60:62-3(1948).

30. Fernholz, H., Chem. Ber. 84:110-22(1951).

31. Ibne-Rasa, K. M., and Edwards, J. O., J. Am. Chem. Soc. 84:763-8(1962).

32. Schumb, W. C., Satterfield, C. N., and Wentworth, R. L. Hydrogen peroxide. New York, Reinhold Publishing Corp., 1955. 759 p.

33. Leffler, J. E., J. Org. Chem. 16:1785-7(1951).

34. Kwart, H., and Wegener, N. J., J. Am. Chem. Soc. 83:2746-55(1961).

35. Henderson, G. G., and Boyd, R., J. Chem. Soc. 97:1659-69(1910).

36. Hamilton, G. A., Friedman, J. P., and Campbell, P. M., J. Am. Chem. Soc. 88:5266-8(1966).

37. Thompson, N. S., and Kaustinen, O. A., Tappi 47:157-62(1964).

38. Neimo, L., Baczynska, K., and Sihtola, H., Paper and Timber 47:43-50, 54-8 (1965).

39. Poljak, A., Ang. Chem. A60:45-6(1948).

40. Haas, V. H., Schoch, W., and Strole, U., Das Papier 9:469-75(1955).

41. Taniguchi, E., J. Japan. Tappi 19:283-7(1965); A.B.I.P.C. 36:4858.

42. Ishikawa, H., Okubo, K., and Oki, T., J. Japan. Tappi 20:485-90(1966); A.B.I.P.C. 37:8914.

43. Ishikawa, H., Kinoshita, Y., Oki, T., and Okubo, K., J. Japan. Tappi 21:494-500(1967).

44. Sarkanen, K. V., and Suzuki, J., Tappi 48:459-64(1964).

45. Lai, Y., and Sarkanen, K. V., Tappi 51:449-53(1968).

46. Poljak, A., German pat. 1,013,285(Aug. 8, 1957); C.A. 53:22949a.

47. Wacek, A., U. S. pat. 2,534,212(Dec. 19, 1950).

48. Pauly, H., Gilmour, R., and Will, G., Ann. 403:119-67(1914).

49. Bible, R. H. Interpretation of NMR spectra. p. 77-104. New York, Plenum Press, 1965. 150 p.

50. Garbisch, E. W., J. Chem. Ed. 45:402-16(1968).

51. Silverstein, R. M., and Bassler, G. C. Spectrometric identification of organic compounds. 2nd ed. p. 4-63. New York, John Wiley & Sons, Inc., 1967.

52. Ref. (51), p. 138.

53. Friedman, L., and Long, F. A., J. Am. Chem. Soc. 75:2832-6(1953).

54. Piskov, V. B., Zhur. Obshchei Khim. 30:1390-5(1960).

55. Shaw, E., J. Am. Chem. Soc. 68:2510-13(1946).

56. Kittila, R. S. Dimethylformamide chemical uses. Wilmington, Delaware, E. I. du Pont de Nemours & Co., 1967.

57. Klebe, J. F., Finkbeiner, H., and White, D. M., J. Am. Chem. Soc. 88:3390-5 (1966).

58. Ref. (51), p. 110-47.

59. Karrer, P., Schwyzer, R., and Neuwirth, A., Helv. Chim. Acta 31:1210-14(1948).

60. Morgan, L. R., J. Org. Chem. 27:1208-10(1962).

61. Boeseken, J., and Sloof, G., Rec. Trav. Chim. 49:91-4(1930).

62. Boeseken, J., and Konigsfeldt, J. M. L., Rev. Trav. Chim. 54:313-16(1935).

63. Fernholz, H., and Piazlo, G., Chem. Ber. 87:578-81(1954).

64. Sadtler Research Laboratories, 1517 Vine Street, Philadelphia, Pa.

65. Viel, C., Arnaud, J. M., Dorme, R., Cheutin, A., and Rumpf, P., Bull. Soc. Chim. Fr. 1967:431-40.

66. Bamberger, E., Ber. 36:2028-41(1903).

67. Derkosch, J., and Kaltenegger, W., Monatsh. Chem. 90:877-84(1959).

68. Budzikiewicz, H., Djerassi, C., and Williams, A. H. Mass spectrometry of organic compounds. San Francisco, Holden-Day, Inc., 1967.

69. Ref. (68), p. 258-65.

70. Beckering, W., and Fowkes, W. W. (U. S. Bur. of Mines, Grand Forks, N. D.) U. S. Bur. Mines Rept. Invest. No. 5505, 1959. 100 p.

71. Hine, J. Physical organic chemistry. p. 87, 372. New York, McGraw-Hill Book Co., Inc., 1962.

72. Fieser, L. F., and Fieser, M. Organic chemistry. 3rd ed. p. 216. New York, Reinhold Publishing Corp., 1956.

73. Kharasch, M. S., Fono, A., Nudenberg, W., and Poshkus, A. C., J. Org. Chem. 15:775-81(1950).

74. Corbett, J. F., J. Chem. Soc. 1966:2308-11.

75. Hawthorne, M. F., Emmons, W. D., and McCallum, K. S., J. Am. Chem. Soc. 80:6393-8(1958).

76. Ref. (72), p. 713.

77. Pearl, I. A., Chem. Eng. News 42, no. 27:81-93(July 6, 1964).

78. Horner, L., and Burger, T., Ann. Chem. 708:105-26(1967).

79. Pauly, H., Gilmour, R., and Will, G., Ann. 403:119-67(1914).

80. FMC Corporation. The operation of a bench scale peracetic acid generator. New York, 1963.

81. Kesler, R. B. Personal communication, 1968.

82. Ledaal, T., and Bernatek, E., Anal. Chem. Acta 28:322-6(1963).

83. Sully, B. D., and Williams, P. L., J. Chem. Soc. 1962:653-7.

84. Phillips, B., Frostick, F. C., Jr., and Starcher, P. S., J. Am. Chem. Soc. 79:5982-6(1957).

85. Havel, S., Sb. Ved. Pr., Vys. Sk. Chem.-Technol., Pardubice 13:31-60(1966); C.A. 67:53325Z.

86. Pecsok, R. L. Principles and practices of gas chromatography. p. 136-50. London, Chapman and Hall, Ltd., 1959.

87. Ref. (72), p. 310.

88. Patchett, A. A., and Witkop, B., J. Org. Chem. 22:1477-84(1957).

89. Ref. (72), p. 324.

90. Frost, A. A., and Pearson, R. G. Kinetics and mechanism. 2nd ed. p. 8-26. New York, John Wiley & Sons, Inc., 1961.

APPENDIX I

POSSIBLE CAUSES OF INCOMPLETE PRODUCT ANALYSIS

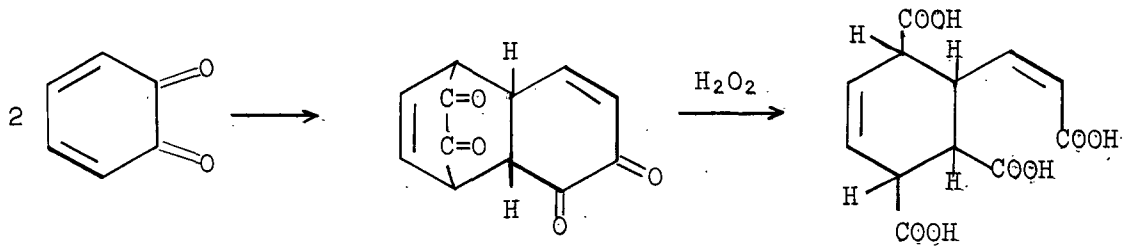
The work-up procedure used in this study was found to be reasonably complete. Work-up controls gave 85% recovery of β-methyl-lactone and 92% recovery of 2-methoxy-5-methyl-p-benzoquinone. The 4-methylpyrocatechol oxidation products that were worked up as normal gave yields about 10-15% lower than those products that were simply concentrated and analyzed. Thus, the quantitative product results were probably not more than 15% low.

Another possible cause of the low product yields would be the many unknown products that were present in very small amounts. These were found in all reaction products but were too small to be detected under normal conditions. Although individually these unknowns account for very little, collectively they may amount to several percent of the product. Also, oxidation of the 2-methoxy-5-methyl-p-benzoquinone product was shown to probably account for a large portion of the missing product in the p-methylanisole oxidation.

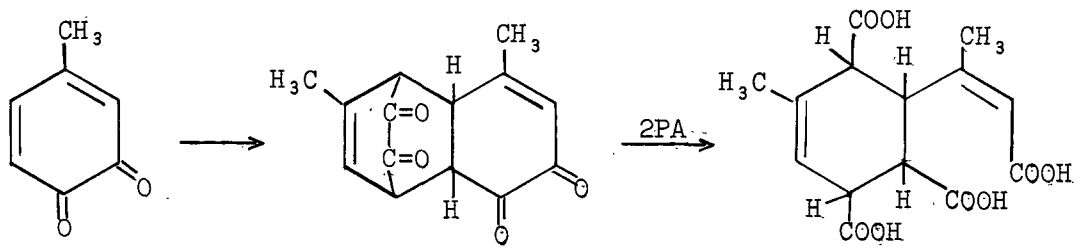
These are the obvious causes for the low product yields. The remaining undetected products would seem to be high molecular weight compounds that could not be analyzed by the gas chromatographic methods used.

QUINONES

A likely cause of the low product yields would be the o-quinone intermediate. o-Quinones are very sensitive to moisture and rapidly decompose (78). In addition, o-quinones are prone to form dimers via the Diels-Alder reaction (87). Patchett and Witkop (88) found that o-benzoquinone in ether containing hydrogen peroxide formed a dimer readily. Dimerization was believed to occur before oxidation by hydrogen peroxide to the tetracarboxylic acid:



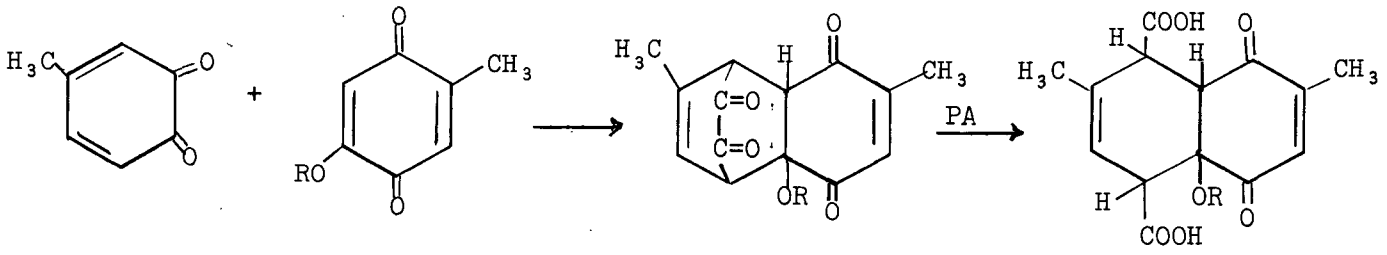
The equivalent dimerization and oxidation of 4-methyl-o-benzoquinone would then proceed as follows:



A large molecule like this with four carboxyl groups would probably not be volatile enough for gas chromatography in either its methylated or silylated form. This could be one reason that the 4-methyl-o-benzoquinone oxidation gave a maximum yield of only 70% when worked up immediately after reaction.

Hydroxy-p-quinones, although reasonably stable, can also dimerize. Corbett (74) found that 2-methyl-5-hydroxy-p-benzoquinone formed a dimer when present in concentrations greater than 10^{-3}M. However, the exact conditions necessary for dimerization are not well known. Tautomerism to the o-quinone may be partly responsible for this dimerization.

The presence of an o-quinone and a p-quinone together in the same solution would seem to favor dimerization between the two. p-Quinones are known to be good dienophiles (87) and would very likely form a dimer with the o-quinone (diene):

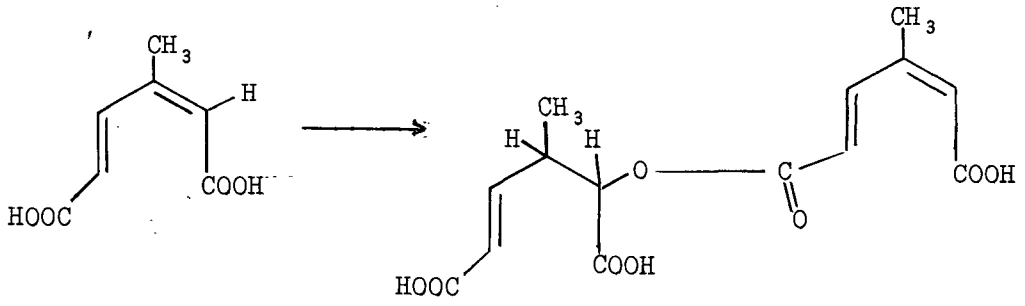


The methyl or trimethylsilyl esters of this oxidation product would probably not be very volatile either.

Thus, there are several ways in which the quinone products could be responsible for forming undetectable materials.

INTERMOLECULAR ESTERIFICATION

Muconic acids can form lactone rings as a result of a carboxyl group joining with an unsaturated carbon. It would seem possible that this same basic reaction could also take place between molecules:

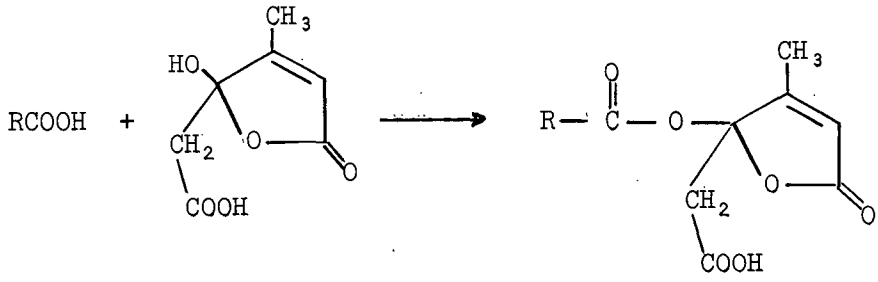


This is only one example of an "intermolecular esterification" reaction that could probably take many different forms. Also, esterification of this type could result in a polymer made up of more than two original molecules.

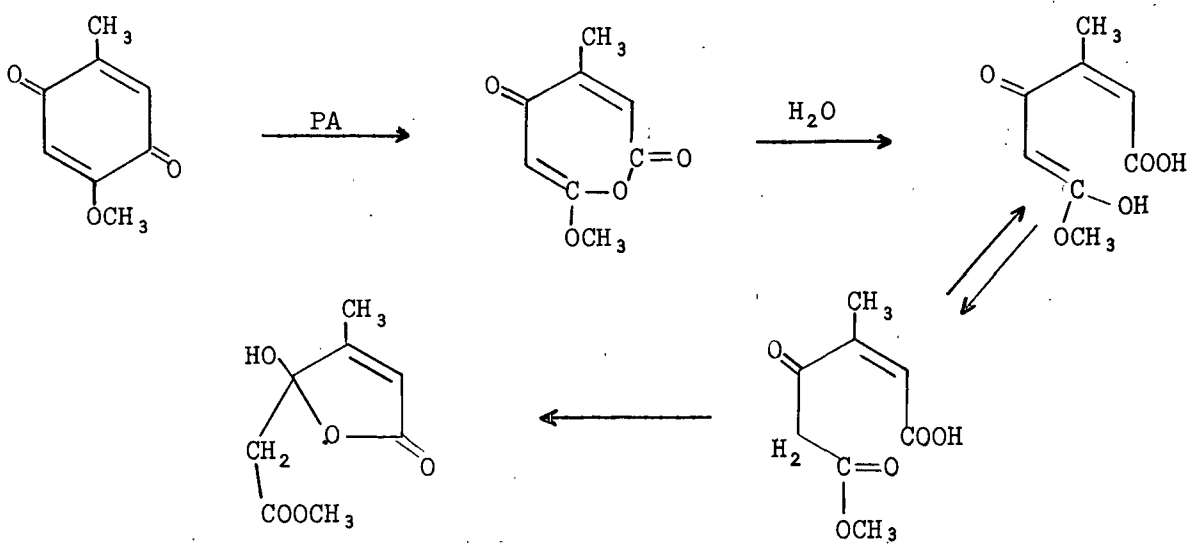
The overall yield of muconic acids from the 4-methyl-o-benzoquinone oxidation decreased from 70 to 55% when the products were stored in the oxidation solution

for 26 hours. Since the muconic acids have been shown to be stable to peroxyacetic acid, the original products must have rearranged to other forms that could not be detected. Some rearrangement of the initial products obviously took place because unknown U2, U3, and U4 were only present in the solution that had been stored 26 hours; these were not present in the product that was worked up immediately after reaction. These results, thus, are an indication that some form of intermolecular esterification may indeed be occurring.

In products containing the hydroxy-lactone, another type of intermolecular esterification might take place: condensation of a carboxyl group on one molecule with the hydroxyl group of γ-hydroxy-lactone. Based on the ease of lactone formation in a γ-hydroxy acid (89), this type of esterification may even be favored over others. R could be any carboxylic acid product in the system.



Finally, one known reason for some of the missing products is the oxidation of 2-methoxy-5-methyl-p-benzoquinone in the p-methylanisole and 4-methylveratrole oxidation products. When this p-quinone was run alone and worked up, no products were found. Since a stoichiometry only slightly greater than 1.0 was found, oxidation to smaller fragments could not occur because a stoichiometry of at least 2.0 would be required. One possible explanation is a Baeyer-Villiger oxidation at a carbonyl group. If this proceeded as previously described for a hydroxy-p-quinone, the following reaction might take place:



This same type of reaction could also be possible at the other carbonyl group, with oxygen insertion on either side. However, no significant products were detected.

As a result of this discussion, it appears that there are many possible ways in which low product yields could occur. Although there is little evidence for any one explanation, many of these taking place at once in the same solution could account for the missing products.

APPENDIX II

POSSIBLE CAUSES OF HIGH STOICHIOMETRY RESULTS

The previously described esterification possibilities may also help to explain the high stoichiometry results. A certain product may be converted to an undetectable form to a greater degree than other products. The resulting detected product mixture could then indicate a different stoichiometry than is actually the case.

The following table shows the experimental stoichiometry found from each reaction and the predicted value based on product yields. The o-quinone, catechol, and p-cresol oxidations gave the stoichiometries predicted.

TABLE XXX

STOICHIOMETRY RESULTS AND PREDICTIONS

Substrate	Stoichiometry		%
	Experimental	Predicted	Reaction
4-Methyl-o-quinone	∿1.0	1.0	100
4-Methylpyrocatechol	2.1	2.0	100
2-Methoxy-p-cresol	3.0	2.4	85
4-Methylveratrole[a]	2.9	2.0	80
p-Cresol	2.7	2.6	60
p-Methylanisole[a]	3.0	2.3	45

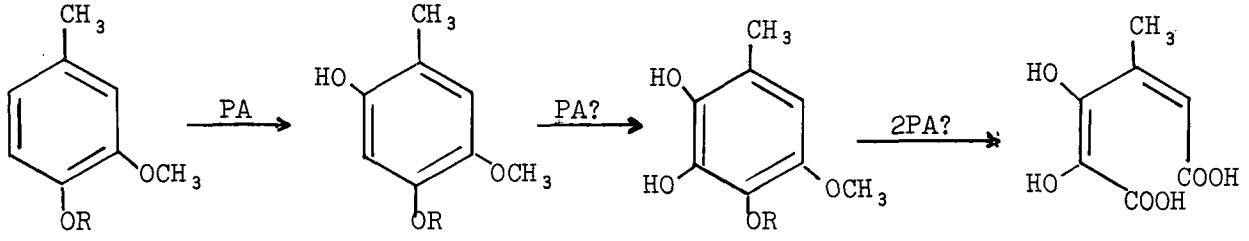
[a]Stoichiometry increased with degree of reaction.

Although the p-methylanisole stoichiometry figures do not agree, this difference could be accounted for on the basis of known products. The oxidation of the p-quinone product has been discussed as a probable main cause of the stoichiometry differences and the increasing value. The γ-hydroxy-lactone product, which requires four moles of peroxyacid for formation, might account for the rest. A previous discussion showed

that the hydroxy-lactone may esterify more easily than other products because of the hydroxyl group. Thus, if most of this product was in an undetectable form, stoichiometry calculations based on the detected products would give an erroneously low figure.

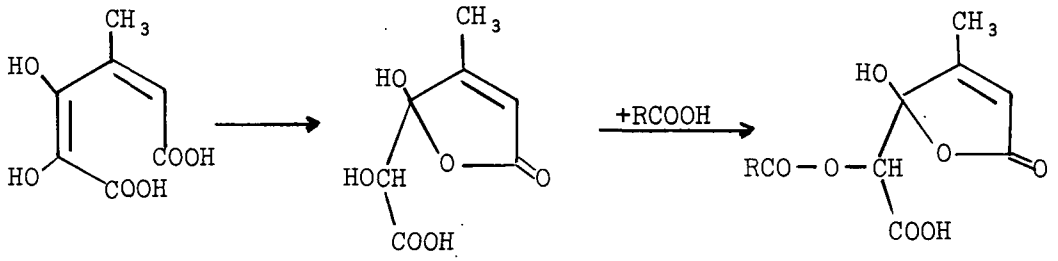
However, the stoichiometry results of the 4-methylveratrole and 2-methoxy-p-cresol oxidations cannot be explained by the identified products: a product requiring four moles of peroxyacid would be needed. Since both methanol and methyl acetate, possible oxidation products, were found to be stable, the only other simple explanation would be oxidative removal of a methoxyl group. But, the p-methylanisole results gave no indication of oxidative demethoxylation. Also, if it is assumed that an extra mole of peroxyacid is required to remove a methoxyl, the subsequent predicted stoichiometry would be significantly higher than what was found experimentally. Therefore, the only other apparent possible cause of the stoichiometry problems would be the missing products.

Since the C-2 methoxyl is unique to 4-methylveratrole and 2-methoxy-p-cresol, it may be an indirect cause of the missing products. It was shown earlier that the presence of methoxyl groups at the C-2 and/or C-1 ring positions promoted hydroxylation at the C-5 position much more than a hydroxyl group. The 5-hydroxy intermediate may then promote oxidation at the C-6 position because of activation by the ortho C-1 and C-5 groups. The entire oxidation sequence might proceed as follows:



This reaction would require four moles of peroxyacid. Thus, if a reaction of this type occurred to a great enough extent, it would explain the high stoichiometry results.

Furthermore, the dihydroxy acid may form undetectable products. This acid, if a real product, would first form a dihydroxy-lactone. This lactone could then probably esterify with another molecule at either hydroxyl group and thus might



never be found in its original form. In this way, it could also tie up a large quantity of muconic acid products and thus might be responsible for the low yields of muconic acids from all methoxyl-containing substrates. This reaction may also take place in the p-methylanisole oxidation.

The formation of this dihydroxy intermediate may also explain the increasing stoichiometry in the 4-methylveratrole oxidation. At longer reaction times, tertiary reactions such as this may become more important as the overall reaction slows down. Thus, an increase in formation of a product requiring a stoichiometry of four (compared to two or three for the other products) would cause an increase in stoichiometry.

However, it would also be possible for this product to be formed in all other oxidation products since the 5-hydroxy intermediate was common to all. Apparently, the C-2 methoxyl is responsible, possibly by inhibiting formation of the quinone intermediates just enough to allow another hydroxylation step.

These explanations for the lack of agreement between observed and predicted stoichiometry are strictly hypothetical. However, they do tend to agree with the observed findings and serve to indicate the type of reactions that could be occurring.

APPENDIX III

ATTEMPTED KINETIC MEASUREMENTS

An attempt was made to determine the reaction order of the peroxyacetic acid oxidation of p-cresol in order to gain more information concerning the reaction mechanism. The p-cresol oxidation was chosen for study because it was the only reaction that had a constant stoichiometry with time and still reacted slow enough to follow titrimetrically.

The influence of the p-cresol concentration on the rate of reaction was studied initially. Peroxyacid to p-cresol molar ratios of 3:1 and 6:1 were used. The reactions were made up and run exactly as described in the experimental section. Aliquots (1.0 ml.) were removed at various intervals and titrated to follow the consumption of peroxyacetic acid with time. A control flask containing only peroxyacetic acid was run at the same time and also titrated. The results of these oxidations are shown in Table XXXII.

An attempt was made to determine whether the p-cresol oxidation was acid-catalyzed: sulfuric acid (0.5%) was mixed into an otherwise standard p-cresol oxidation solution, and the consumption of peroxyacetic acid was followed titrimetrically. A p-cresol oxidation was also run in the presence of methyl methacrylate (3%) and studied in the same manner. In addition to these oxidations, the following controls were run: (a) peroxyacetic acid + sulfuric acid (0.5%), (b) peroxyacetic acid + methyl methacrylate (3%), (c) peroxyacetic acid + p-cresol, and (d) peroxyacetic acid alone. All of these reactions were run in freshly passivated flasks; the results are shown in Table XXXIV.

The resulting data from these reactions were corrected for the relative total solution weight and the spontaneous peroxyacid decomposition as explained before

each table. Column "C" in each table shows the final corrected value for peroxyacetic acid remaining in solution at the indicated time.

The results of these oxidations, both corrected and uncorrected, were then calculated and plotted as several different reaction orders: first order in peroxyacid, second order in peroxyacid, first order in both peroxyacid and p-cresol, second order in peroxyacid and first order in p-cresol (90). The corrected results were viewed with some skepticism because of the odd behavior of the sulfuric acid and methyl methacrylate control flasks used for correction. Therefore, the uncorrected results were also analyzed with the possibility that they might give useful results. A computer program (Table XXXV) was written to plot all of the reactions in these four different ways.

Because the amount of p-cresol consumed was not determined, the theoretical amount was calculated from the peroxyacetic acid concentration data using the previously determined stoichiometry. But since the stoichiometry of the p-cresol oxidation was found to vary with different batches of peroxyacetic acid, stoichiometry values from 2.4 to 3.0 (in increments of 0.1) were used with each set of data to see if a correlation could be found. The program was run on an IBM Model 1620 Computer.

EVALUATION OF RESULTS

All efforts to find the order of any of the reactions gave inconsistent results. The data from each oxidation were found to fit at least two different reaction orders, depending on the value used for stoichiometry. Therefore, no quantitative results could be found concerning the reaction rates or reaction orders of any of the oxidations run.

However, some qualitative observations can be made:

1. The rate of consumption of peroxyacetic acid increased with higher p-cresol concentration (Table XXXII) meaning that p-cresol does enter into the rate equation. Thus, the rate determining step involves p-cresol.

2. Comparison of the uncorrected results of the oxidation containing sulfuric acid (79-1) to those of the control oxidation (79-5) in Table XXXIV indicates that any acid catalysis effect is not very large if present. However, the odd behavior of the sulfuric acid control makes it impossible to draw any definite conclusions.

CORRECTION OF TITRIMETRIC DATA

Since the three oxidations shown in Table XXXI contained varying amounts of p-cresol, the original peroxyacid solution (25 ml.) was diluted to different degrees. Therefore, the two reactions containing p-cresol had to be converted to the same total weight basis as the control reaction by multiplying the peroxyacid results by the ratio of "total solution weights." The correction factors used are shown in Table XXXI.

TABLE XXXI

CONVERSION FACTORS FOR p-CRESOL OXIDATIONS

Reaction Number	Total Solution Weight, g.	p-Cresol Added, g.	Conversion Factor
2675-70-3	28.893	1.9521	1.072
2675-70-4	27.908	0.9667	1.036
2675-70-5	26.941	--	1.000

The converted figures were then further corrected by adding to each figure the corresponding change in peroxyacid concentration from the control flask, thus giving the final corrected value for peroxyacetic acid (Column "C" in Tables XXXII and XXXIV).

TABLE XXXII

TITRIMETRIC RATE DATA FOR p-CRESOL OXIDATION

2675-70-3				2675-70-4				2675-70-5		
Time, hr.	AcO_2H, %			Time, hr.	AcO_2H, %			Time, hr.	AcO_2H, %	
	A	B	C		A	B	C		A	Correction
0	9.53	10.22	10.22	0	9.87	10.22	10.22	0	10.22	0
3.0	7.99	8.57	8.68	3.1	8.97	9.29	9.40	3.3	10.11	0.11
6.3	6.69	7.17	7.33	6.3	8.21	8.51	8.67	6.5	10.06	0.16
9.0	5.84	6.26	6.49	9.0	7.66	7.94	8.17	9.2	9.99	0.23
13.0	4.89	5.24	5.55	13.0	7.00	7.25	7.56	13.1	9.91	0.31
18.0	4.02	4.31	4.74	18.0	6.33	6.56	6.99	18.2	9.79	0.43
24.1	3.19	3.42	3.97	24.2	5.66	5.86	6.41	24.3	9.67	0.55
30.0	2.60	2.79	3.46	30.0	5.16	5.35	6.02	30.1	9.55	0.67
37.0	2.08	2.23	3.03	37.0	4.67	4.84	5.64	37.2	9.42	0.80
47.6	1.52	1.63	2.61	47.2	4.11	4.26	5.24	47.3	9.24	0.98
55.1	1.25	1.34	2.45	55.2	3.78	3.92	5.03	55.4	9.11	1.11

A = Initial titrated value.

B = Value converted to base weight of control.

C = Final value corrected for control decomposition.

The data in Table XXXIV were corrected in the same manner as Table XXXII. However, in this case, there was a control reaction for each oxidation. Thus, the results for 79-1, 79-3, and 79-5 had to be converted separately to the same solution weight as their individual controls and then corrected by the amount of decomposition in that same control (79-2, 79-4, and 79-6, respectively) (Table XXXIII).

TABLE XXXIII

CONVERSIONS BASED ON TOTAL SOLUTION WEIGHT

Reaction Number	Total Solution Weight, g.	p-Cresol Added, g.	Conversion Factor
2675-79-1[a]	27.983	1.005	1.037
2675-79-2[a]	26.978	--	--
2675-79-3[b]	28.788	1.001	1.036
2675-79-4[b]	27.787	--	--
2675-79-5	27.853	1.002	1.037
2675-79-6	26.851	--	--

[a]Contained 0.5% sulfuric acid.

[b]Contained 3% methyl methacrylate.

TABLE XXXIV

TITRIMETRIC RATE DATA

Time, hr.	p-Cresol Oxidation AcO_2H, % A	B	C	Time, hr.	Control AcO_2H, % A	Correction
	2675-79-1 (H_2SO_4)				2675-79-2 (H_2SO_4)	
0	9.74	10.10	10.10	0	10.10	--
3.4	8.31	8.62	9.42	3.4	9.30	0.80
8.0	6.84	7.09	8.51	8.2	8.68	1.42
14.0	5.68	5.89	7.72	13.9	8.27	1.83
20.1	4.90	5.08	7.12	20.1	8.06	2.04
27.3	4.32	4.48	6.60	27.4	7.98	2.12
36.0	3.81	3.95	6.12	36.1	7.93	2.17
45.6	3.40	3.53	5.70	45.6	7.93	2.17
53.7	3.13	3.25	5.44	53.8	7.91	2.19
	2675-79-3 (Methacrylate)				2675-79-4 (Methacrylate)	
0	9.47	9.81	9.81	0	9.81	--
3.6	8.40	8.70	9.30	3.9	9.21	0.60
8.6	7.37	7.64	8.94	8.7	8.51	1.30
14.4	6.42	6.65	8.67	14.5	7.79	2.02
20.5	5.65	5.85	8.59	20.7	7.07	2.74
27.7	4.97	5.15	8.70	27.7	6.26	3.55
36.4	4.33	4.49	8.89	36.4	5.41	4.40
45.9	3.80	3.94	9.15	45.9	4.60	5.21
54.1	3.46	3.58	9.39	54.1	4.00	5.81
	2675-79-5 (p-Cresol only)				2675-79-6	
0	9.78	10.15	10.15	0	10.15	--
4.1	8.89	9.22	9.33	4.3	10.04	0.11
9.0	7.57	7.85	8.05	9.1	9.95	0.20
14.8	6.54	6.78	7.11	14.9	9.82	0.33
20.9	5.78	5.99	6.44	21.0	9.70	0.45
28.0	5.09	5.28	5.87	28.1	9.56	0.59
36.6	4.46	4.63	5.38	36.7	9.40	0.75
46.2	3.95	4.10	5.00	46.3	9.25	0.90
54.4	3.61	3.74	4.76	54.4	9.13	1.02

A = Initial titrated value.

B = Value converted to base weight of control.

C = Final value corrected for control decomposition.

TABLE XXXV

COMPUTER PROGRAM USED TO CALCULATE REACTION RATES

```
C          Calculation and plot of p-cresol oxidation kinetic data dimension
     X (20), Y (20), IX (40), IY (40), INAME (40), AK (20), A (20), B (20)
     Dimension APA (40)
     Read 106, IXN, (IX(I),I=1, IXN)
     Read 106, IYN, (IY(1),I=1, IYN)
   1 Read 103, NRXN, NO, N. WTPA, XML, AO, BO
     Read 102, (X(I),APA(I),I=1,N)
     AO = AO*WTPA/7605./XML
     BO = BO/108.1/XML
   2 Read 102,S
     DO 11 I=1,N
     A(I) = APA(I)*WTPA/7605./XML
     B(I) = BO - (AO-A(I))/S
  11 Continue
     Pause
     IF (sense switch 1) 17,12
  12 Pause
     IF (sense switch 2) 22,19
  19 Pause
     IF (sense switch 3) 20,24
C          First-order plot   A =
  17 DO 18 I=1,N
     B(I) = 0.
     Y(I) = (2.303)*log(AO/A(I))
     AK(I) = Y(I)/X(I)
  18 Continue
     Print 129
     Go to 26
C          Second-order plot   2A =
   2 DO 23 I=1,N
   2 B(I) = 0.
     Y(I) = 1./A(I) - 1./AO
     AK(I) = Y(I)/X(I)
  23 Continue
     Print 130
     Go to 26
C          Second-order plot   A + B =
  20 DO 21 I=1,N
     Y(I) = (S/(S*BO-AO))*(2.303)*log((AO*B(I))/(BO*A(I)))
     AK(I) = Y(I)/X(I)
  21 Continue
     Print 131
     Go to 26
```

TABLE XXXV (Continued)

COMPUTER PROGRAM USED TO CALCULATE REACTION RATES

```
C               Third-order plot  2A + B =
   24 DO 25 I=1,N
      Const = S*BO - AO
      C = (S/Const)*(1./A(I) - 1./AO)
      D = (S/(Const**2))*((2.303)*log((BO*A(I))/(AO*B(I))))
      Y(I) = C + D
      AK(I) = Y(I)/X(I)
   25 Continue
      Print 132
C               Data output
   26 Print 140, NRXN, NO, S
      Print 120
      Print 121,(I,X(I),A(I),B(I),Y(I),AK(I),I=1,N)
C               Plot of data
   13 Call plot (0.,-11.,3)
      Call plot (0.,-9.,-3)
      Call scale(X,5.5,N,1)
      Call scale(Y,7.,N,1)
      Call axis (0.,0.,IX,-IXN,5.5,0.,X(N+1),X(N+2))
      Call axis(0.,0.,IY,IYN,7.,1.5707963,Y(N+1),Y(N+2))
      Call line(X,Y,N,1,-1,2)
      Call plot (11.5,0.,-3)
      Go to 1
C               I/O statements
  101 Format (I5)
  102 Format(8F10.5)
  103 Format(3I5,4F10.5)
  106 Format(I5,30A2)
  120 Format(/6X,1H   I,3X,8HTIME,HR.,2X,7HPERACID,3X,9HSUBSTRATE,6X,
      12HKT,6X,13HRATE CONSTANT/)
  121 Format(4X,I3,3X,F5.1,5X,F6.3,5X,F6.3,3X,E12.5,2X,E12.5)
  129 Format(//20X,20H1ST-ORDER PLOT IN PA)
  130 Format(//20X,20H2ND-ORDER PLOT IN PA)
  131 Format(//20X,31H2ND-ORDER PLOT IN PA + P-CRESOL)
  132 Format(//20X,31H3RD-ORDER PLOT IN PA + P-CRESOL)
  140 Format(20X,12HREACTION NO.,I4,1X,1H-,I2,6X,3HS = ,1X,F6.3)
      END
               S = Stoichiometry
      X(I) = Reaction time
      WTPA = Weight of peracid solution
       XML = Original peracid concentration
      A(I) = Peracid concentration at time X(I)
        BO = Original grams p-cresol added
      B(I) = Calculated p-cresol concentration
```

APPENDIX IV

DETERMINATION OF WEIGHT RESPONSE FACTORS

This appendix contains the weight response factor data for all starting materials and those products that were available in large enough amounts for evaluation. These response factors were determined by weighing the substrate and internal standard into a small flask and dissolving in a suitable solvent (ether or benzene). Three or four injections into the gas chromatograph were usually made under the appropriate conditions. The results that were triangulated are reported to two decimal places and usually are numerically no greater than 30.00, while the integrated results are normally in the hundreds (one-decimal place) (Tables XXXVI-XLV). The response factors were determined at least once because of use of a new column or gas chromatograph.

TABLE XXXVI

4-METHYLPYROCATECHOL WEIGHT RESPONSE FACTOR[a]

Area, $cm.^2$		$cm.^2/g.$		Response Factor
p-MP	4-MC	p-MP	4-MC	F
0.1263 g. p-methoxyphenol, 0.1019 g. 4-methylpyrocatechol				
7.94	4.58	62.87	44.94	1.399
15.91	9.56	126.0	93.82	1.343
11.39	7.77	90.18	76.25	1.183
0.1263 g. p-methoxyphenol, 0.1513 g. 4-MC				
12.90	11.90	102.1	78.65	1.299
13.47	11.96	106.6	79.05	1.349
20.47	18.94	162.1	125.2	1.295
		Av. F = 1.31		

[a]Run on Apiezon L column at 122° and 120 ml./min. He flow rate.

TABLE XXXVII

p-METHYLANISOLE WEIGHT RESPONSE FACTOR

Area, $cm.^2$		$cm.^2/g.$		Response Factor
Anisole	p-MA	Anisole	p-MA	F
0.3978 g. anisole, 0.4112 g. p-methylanisole[a]				
12.31	11.82	30.95	28.75	1.077
11.05	11.12	27.78	27.04	1.027
9.33	9.30	23.45	22.62	1.037
Av. F = 1.047				
Area		Area/gram		
0.5397 g. anisole, 0.6627 g. p-methylanisole[b]				
237.8	275.8	440.6	416.2	1.059
227.9	275.4	422.3	415.6	1.016
229.2	284.7	424.7	429.6	0.989
312.7	376.2	579.4	567.7	1.021
Av. F = 1.021				

[a] Run on Carbowax 20M column at 80° and 170 ml./min. He flow rate.

[b] Run on new Carbowax 20M column at 70° and 120 ml./min. He flow rate.

TABLE XXXVIII

p-CRESOL WEIGHT RESPONSE FACTORS

Area, $cm.^2$		$cm.^2/g.$		Response Factor
Phenol	p-Cresol	Phenol	p-Cresol	F
	0.3009 g. phenol, 0.2457 g. p-cresol[a]			
23.12	18.18	76.84	73.99	1.039
18.44	15.01	61.28	61.09	1.003
18.69	14.59	62.11	59.38	1.046
	Av. F = 1.029			
	0.1095 g. phenol, 0.1820 g. p-cresol[b]			
14.99	23.07	136.9	126.8	1.080
15.04	24.19	137.4	132.9	1.034
15.32	24.55	139.9	134.9	1.037
	0.1812 g. phenol, 0.1820 g. p-cresol[b]			
24.85	23.63	137.1	129.8	1.056
21.66	20.84	119.5	114.5	1.044
19.60	18.89	108.2	103.8	1.042
19.97	18.94	110.2	104.1	1.059
	Av. F = 1.050			
Area		Area/gram		
	0.3203 g. phenol, 0.4052 g. p-cresol[c]			
255.2	304.8	796.8	752.2	1.059
199.9	247.5	624.1	610.8	1.022
181.7	227.0	567.3	560.2	1.013
212.5	254.3	663.4	627.6	1.057
			Av. =	1.038

[a] Run on didecyl phthalate at 145° and 180 ml./min. He flow rate.
[b] Run on Carbowax 20M at 150° and 75 ml./min. He flow rate.
[c] Run on new Carbowax 20M at 150° and 120 ml./min. He flow rate.

TABLE XXXIX

4-METHYLVERATROLE WEIGHT RESPONSE FACTOR

Area, cm.^{2}		cm.^{2}/g.		Response Factor
p-DB	4-MV	p-DB	4-MV	F
0.2388 g. p-dimethoxybenzene, 0.2707 g. 4-methylveratrole[a]				
29.89	33.19	125.2	122.6	1.021
25.15	27.39	105.3	101.2	1.041
25.30	27.79	105.9	102.7	1.031
Av. F = 1.031				
0.1160 g. p-dimethoxybenzene, 0.1115 g. 4-methylveratrole[b]				
17.02	15.14	146.7	135.8	1.080
17.32	15.82	149.3	141.9	1.052
17.15	16.34	147.8	146.5	1.009
18.25	16.21	157.3	145.4	1.082
same amount veratrole, 0.1645 g. 4-methylveratrole[b]				
12.92	17.41	111.4	105.8	1.053
14.63	19.68	126.1	119.6	1.054
14.39	19.15	124.1	116.4	1.066
14.93	20.33	128.7	123.6	1.041
Av. F = 1.055				

[a] Run on didecyl phthalate at 150° and 75 ml./min. He flow rate.

[b] Run on Carbowax 20M at 130° and 80 ml./min. He flow rate.

TABLE XL

4-METHYLVERATROLE WEIGHT RESPONSE FACTOR

Area		Area/gram		Response Factor
p-DB	4-MV	p-DB	4-MV	F
0.1670 g. p-dimethoxybenzene, 0.2468 g. 4-methylveratrole[a]				
140.8	193.7	843.1	784.8	1.074
141.2	196.0	845.5	794.2	1.065
136.8	189.8	819.2	769.0	1.065
		Av. F = 1.068		
same solution as above[b]				
233.4	334.6	139.8	135.6	1.031
236.5	338.2	141.6	137.0	1.083
228.0	307.8	136.5	124.7	1.095
		Av. F = 1.070		

[a] Run on new Carbowax 20M and temperature programmed from 100 to 160° at 2°/min. and 120 ml./min. He flow rate.

[b] Run on new Carbowax 20M at 125° and 120 ml./min. He flow rate.

TABLE XLI

2-METHYL-5-METHOXY-p-BENZOQUINONE
WEIGHT RESPONSE FACTOR

Area, cm.^{2}		cm.^{2}/g.		Response Factor
p-MP	p-Q	p-MP	p-Q	F
0.0982 g. p-methoxyphenol, 0.0874 g. 2-Me-5-MeO-p-quinone[a]				
11.81	5.74	120.3	65.68	1.832
15.84	8.31	161.3	95.08	1.696
16.88	8.77	171.9	100.3	1.714
13.30	6.39	135.4	73.11	1.852
		Av. F = 1.77		
Area		Area/gram		
0.0914 g. p-methoxyphenol, 0.1246 g. 2-Me-5-MeO-p-quinone[b]				
169.7	105.7	185.7	848.3	2.19
191.6	124.3	209.6	997.6	2.10
168.9	110.3	184.8	885.2	2.09
238.9	153.7	261.4	123.4	2.12
329.0	207.9	360.0	166.9	2.16
		Av. F = 2.13		

[a] Run on new Carbowax 20M at 175° and 120 ml./min. He flow rate.

[b] Run on the same Carbowax 20M column under the same conditions but at a later date.

TABLE XLII

2-METHYL-5-METHOXY-*p*-BENZOQUINONE
WEIGHT RESPONSE FACTOR[a]

Area TMB	Area *p*-Q	Area/gram TMB	Area/gram *p*-Q	Response Factor *F*
0.2090 g. trimethoxybenzene, 0.1056 g. 2-Me-5-MeO-*p*-quinone				
474.2	183.9	226.9	174.1	1.303
487.8	182.5	233.4	172.8	1.351
511.3	194.5	244.6	184.2	1.328

Av. *F* = 1.33

[a]Run on SE-30 column at 125° and 75 ml./min. He flow rate.

TABLE XLIII

2-METHOXY-*p*-CRESOL WEIGHT RESPONSE FACTOR[a]

Area Guaiacol	Area MeO-*p*-C	Area/gram Guaiacol	Area/gram MeO-*p*-C	Response Factor *F*
0.3217 g. guaiacol, 0.4342 g. 2-methoxy-*p*-cresol				
181.4	242.2	563.9	557.8	1.011
182.6	229.9	567.6	529.5	1.072
176.6	213.6	549.0	491.9	1.116

Av. *F* = 1.07

[a]Run on new Carbowax 20M column at 140° and 120 ml./min. He flow rate.

TABLE XLIV

β-METHYL-γ-CARBOXYMETHYL-$\Delta^{\alpha,\beta}$-BUTYROLACTONE
WEIGHT RESPONSE FACTOR[a]:
RUN AS TRIMETHYLSILYL DERIVATIVES

Area		Area/gram		Response Factor
Adipic	β-ML	Adipic	β-ML	F
	0.0857 g. adipic acid, 0.1120 g. β-methyl-lactone			
204.5	148.7	238.6	142.7	1.672
185.4	147.6	216.3	131.8	1.641
171.4	137.9	200.0	123.1	1.625
	0.0594 g. adipic acid, 0.1236 g. β-methyl-lactone			
250.3	318.0	421.4	257.3	1.638
231.0	301.1	388.9	243.6	1.596
221.9	281.2	373.6	227.5	1.642
238.8	303.1	402.0	245.2	1.639

Av. F = 1.65

[a]Run on SE-30 column at 165° and 75 ml./min. He flow rate.

TABLE XLV

cis, trans-β-METHYLMUCONIC ACID
WEIGHT RESPONSE FACTOR[a]

Area		Area/gram		Response Factor
Adipic	β-MMA	Adipic	β-MMA	F
0.0857 g. adipic acid, 0.0213 g. β-methylmuconic acid				
204.5	33.9	238.6	185.9	1.242
185.4	35.0	216.3	164.3	1.316
171.4	34.5	200.0	162.0	1.235
		Av. F = 1.28		
0.0536 g. adipic acid, 0.0425 g. β-methylmuconic acid				
235.0	132.5	438.4	311.8	1.406
205.4	117.5	383.2	276.5	1.386
237.6	144.9	443.3	340.9	1.300
208.2	118.2	388.4	278.1	1.397
182.1	108.8	339.7	256.0	1.327
		Av. F = 1.36		

[a]Run on SE-30 column at 165° and 75 ml./min. He flow rate.

APPENDIX V

QUALITATIVE ANALYSIS OF OXIDATION PRODUCTS

The following lists the composition of each column used in the gas chromatographic analyses:

Preparative Carbowax 20M:

20% Carbowax 20M on 60/80 mesh chromosorb W, DMCS treated, acid washed, in 6 ft. x 3/8 in. stainless steel tubing.

Carbowax 20M (C-20M):

15% Carbowax 20M on 60/80 mesh chromosorb W, DMCS treated, acid washed, in 5 ft. x 1/4 in. stainless steel tubing.

SE-30:

20% SE-30 on 60/80 mesh chromosorb W, DMCS treated, acid washed, in 5 ft. x 1/4 in. stainless steel tubing.

Apiezon L (A-L):

20% Apiezon L on 60/80 mesh chromosorb W, DMCS treated, acid washed, in 5 ft. x 1/4 in. stainless steel tubing.

Didecyl Phthalate (D-P)

25% Didecyl phthalate on 60/80 mesh chromosorb W, HMDS treated, in 6 1/2 ft. x 1/4 in. stainless steel tubing.

The Carbowax 20M and SE-30 columns were used in most of the work while the Apiezon L and didecyl phthalate columns were only used for a few analyses at the beginning of the study.

Tables XLVI and XLVII show the retention times of the substrates and products under the GLC conditions most commonly used.

The products denoted U1, U2, U2A, and U5 have not been identified although infrared spectra were obtained for U3 and U4, giving some clue to what the compound might be. These and other spectra are shown in the following tables.

TABLE XLVI

RETENTION TIMES OF SUBSTRATES

Substrate	Retention Time, min.
p-Methylanisole	17.6[a]
4-Methylveratrole	15.5[b]
2-Methoxy-p-cresol	11.8[c]
p-Cresol	12.5[d]
4-Methylpyrocatechol	25.0[e]

[a]Carbowax 20M, 70°, 120 ml./min. He flow rate.
[b]Carbowax 20M, 125°, 120 ml./min. He flow rate.
[c]Carbowax 20M, 140°, 120 ml./min. He flow rate.
[d]Apiezon L, 122°, 120 ml./min. He flow rate.
[e]Didecyl phthalate, 172°, 200 ml./min. He flow rate.

TABLE XLVII

RETENTION TIMES OF NEUTRAL PRODUCTS

	Retention Time, min.			
	C-20M[a]	C-20M[b]	C-20M[c]	SE-30[d]
U1	12.6	--	--	--
Dienone-acetal[e]	17.2	6.2	--	--
2-Hydroxy-p-methylanisole	18.9	7.9	--	--
4-Hydroxy-4-methyl-2,5-cyclohexadienone	27.0	16.3	6.6	--
U5	29.3	19.5	7.6	--
2-Methoxy-5-methyl-p-benzoquinone	∿32	∿22	8.5	--

[a]100-160°, 2°/min., 120 ml. He flow rate.
[b]150°, 120 ml./min. He flow rate.
[c]175°, 120 ml./min. He flow rate.
[d]125°, 75 ml./min. He flow rate.
[e]This product was found to be the result of reaction between acetaldehyde and the dienone.

The spectra in Table XLVIII confirm the 4-methyl-o-benzoquinone structure. At the same time, however, they show that a significant amount of impurity is present.

TABLE XLVIII

INFRARED AND NMR OF 4-METHYL-o-BENZOQUINONE

Infrared		NMR			
$cm.^{-1}$	Intensity	δ, p.p.m.	Splitting	J, c.p.s.	Number of Protons
3065	VW	1.90	2	1.5	1 (Impurity)
3048	W	2.20 (a)	2	1.5	3
3017	VW	2.30	2	1	1 (Impurity)
2956	W	6.35 (b)	2	10.5	2
1735	MW	6.94 (c)	4	10, 2	1
1680	S				
1658	VS				
1622	S				
1567	MS				
1433	S				
1400	VS				
1377	S				
1273	VS				
1123	MS				
1140	M				
808	S				
768	MS				
590	M				
532	MS				

The spectra of U3 and U4 in Table XLIX are very similar, having many identical bands. They also possess what appears to be a typical β-methyl-γ-$\Delta^{\alpha,\beta}$-lactone group of bands from 1640 to 1315 cm.$^{-1}$, which is also present in known β-methyl-lactone. The bands at 3350-3400 cm.$^{-1}$ and 2600 cm.$^{-1}$ identify them as carboxylic acids.

U1, U2A, and U5 were not examined.

TABLE XLIX

INFRARED DATA FOR UNKNOWNS U3 and U4

U3		U4		β-Methyl-lactone	
cm.$^{-1}$	Intensity	cm.$^{-1}$	Intensity	cm.$^{-1}$	Intensity
∿3350	MS (broad)	3390	S (sharp)	3400	M
3118	W	3100	MS	∿3100	M
2960	W	2990	M	2990	M
2922	M	2920	MS	2930	VW
2857	MW	2850	M	--	--
∿2600	M (broad)	∿2600	M	∿2600	W
1735	VS (broad)	1730	VS	1730	VS
				1690	VS
1640	S	1640	S	1640	M
1435	M	1440	MS	1434	MW
1400	W	1400	W	1400	M
1383	M	1383	M	1383	MW
1340	W	1340	W	1340	MW
1315	M	1317	M	1318	M
1260	M	1295	MS	1222	MW
1182	M	1183	S	1178	S
1124	S	1120	VS	--	--
1059	M	1060	MS	1038	M
980	MS	988	MS	987	M
926	M	941	M	932	MW
872	M	876	S	872	W
847	M	792	M	841	M
735	MW	721	M	--	--
670	MS	670	MS	650	MW

APPENDIX VI

QUANTITATIVE ANALYSIS DATA

This appendix contains all of the quantitative data used in calculating the stoichiometry and product yields.

CORRECTIONS

Tables L through LII show various corrections used in calculating final data results. Table L shows the conversion of "grams acetal" into "grams dienone," carried out by multiplying the amount of acetal found by the ratio of the molecular weight of dienone to that of acetal (0.738). Since the acetal was found to form from the dienone during the reduction step in the work-up, this calculation gives what should be the actual yield of the dienone (assuming equal responses).

TABLE L

CONVERSION OF ACETAL INTO DIENONE

Reaction No.	Acetal, g.	Factor	Dienone, g.		Total Dienone, g.
			Calculated	GLC	
2629- 97E	0.128	0.738	0.094	0.028	0.122
102E	0.155	0.738	0.114	0.047	0.161
2675- 13-4	0.017	0.738	0.013	0.071	0.084
25-1	0.106	0.738	0.078	0.007	0.085
25-2	0.121	0.738	0.089	0.004	0.093
87-1E	0.079	0.738	0.058	0.018	0.076
87-2E	0.096	0.738	0.071	0.034	0.105
87-4E	0.174	0.738	0.128	0.024	0.152
128E	0.073	0.738	0.054	0.051	0.105
155-1E	0.144	0.738	0.106	0.016	0.122
155-3E	0.183	0.738	0.135	0.030	0.165
2617- 71E	0.124	0.738	0.092	0.041	0.133

Many reactions were run on which both stoichiometry and product analyses were made. Since titration samples were withdrawn to determine the stoichiometry, the subsequent product data had to be corrected for the product withdrawn. The correction factors used are shown in Table LI and all of the products from these reactions were corrected to give the true yields.

TABLE LI

CORRECTIONS FOR TITRATION SAMPLES WITHDRAWN

Reaction No.	Total Solution Weight, g.	Sample Withdrawn, g.	Remaining Solution, g.	Correction
2675- 13-2	28.803	2.129	26.674	1.080
13-4	28.266	2.133	26.133	1.082
13-5	28.449	2.102	26.347	1.080
70-1	28.274	2.100	26.174	1.080
128	28.434	1.092	27.342	1.040
155-3	29.184	1.081	28.103	1.038
155-1	28.419	1.124	27.295	1.041
2617- 55-2	27.230	1.067	26.163	1.041
62-3	28.675	1.092	27.583	1.040
71	28.527	1.088	27.439	1.040

STOICHIOMETRY RESULTS

Table LII shows the peroxyacetic acid data used to calculate the stoichiometry for each reaction. A sample stoichiometry calculation table is shown in Table LIII. The results for degree of reaction used in calculating stoichiometry and product yields are shown in Table LIV.

TABLE LII

PEROXYACID FIGURES USED IN STOICHIOMETRY CALCULATIONS

Reaction No.	Reaction Time, hr.	Peracid, % Initial	Peracid, %: Final Oxidation	Final Control	Peracid Weight, g. (25 ml.)	H_2O_2, % Initial
			4-Methylpyrocatechol			
2601- 31-1	30	10.08	0.67	9.41	26.898	0.63
31-2	30	10.08	0.61	9.41	26.898	0.63
43-1[a]	16	9.96	0.96	9.72	26.989	0.86
43-2[a]	16	9.96	0.94	9.72	26.989	0.86
49-1[a]	0.5	10.08	2.69	--	27.019	0.9
49-2[a]	0.5	10.01	2.40	--	26.930	0.9
2675- 13-5	22.5	10.24	2.05	9.65	26.954	0.09
			2-Methoxy-p-Cresol			
2617- 62-3	24.3	10.24	0.88	9.70	26.993	0.12
			4-Methylveratrole			
2601- 52[a]	24	10.01	1.77	9.61	26.915	0.9
70-1	24	9.95	1.54	9.81	27.137	2.7
70-2	24	9.95	1.47	9.81	27.137	2.7
157-1	1	10.32	8.42	--	27.021	1.2
144-1	3.5	10.37	6.49	10.36	27.106	0.8
144-2	2.5	10.37	4.58	10.28	27.106	0.8
144-3	13	10.37	3.26	10.19	27.106	0.8
144-4	23.5	10.37	1.94	10.06	27.106	0.8
2675- 13-2	30	10.24	1.21	9.47	26.954	0.09
			2-Methyl-5-Methoxy-p-Benzoquinone			
2629-130-1	48	8.05	7.35	7.95	26.91	1.6
2617- 55-2	50	7.13	6.08	6.61	26.801	0.05

TABLE LII (Continued)

PEROXYACID FIGURES USED IN STOICHIOMETRY CALCULATIONS

Reaction No.	Reaction Time, hr.	Peracid, % Initial	Peracid, %: Final Oxidation	Final Control	Peracid Weight, g. (25 ml.)	H_2O_2, % Initial
			p-Cresol			
2601- 12-1	30	10.41	3.20	9.62	26.862	0.27
12-2	30	10.41	3.20	9.62	26.867	0.27
106-1	6.5	10.31	7.81	10.18	27.022	0.05
106-2	16.5	10.31	5.94	10.01	27.022	0.05
106-3	20.8	10.31	4.65	9.80	27.022	0.05
106-4	40.5	10.31	3.69	9.58	27.022	0.05
2675- 13-4	57	10.24	2.68	8.97	26.954	0.09
70-1	48.5	10.22	2.87	9.11	26.941	0.03
155-3	54	10.40	2.54	9.30	26.941	0.05
			p-Methylanisole			
2601-117-1	6	10.19	9.13	10.04	26.922	0.25
157-2	5.8	10.32	9.23	10.23	27.021	1.1
117-2	16	10.19	8.07	9.88	26.922	0.25
117-3	25	10.19	7.29	9.75	26.922	0.25
117-4	41	10.19	6.04	9.48	26.922	0.25
2675-155-1	72	10.40	4.09	8.91	26.941	0.05
2617- 71	74.5	10.30	4.35	9.33	27.052	1.41

[a]Oxidation run at 23.5°.

TABLE LIII

SAMPLE STOICHIOMETRY CALCULATION

Reaction Product No. 2675-13-2 (4-Methylveratrole)

		Oxidation	Control
1.	10% Peroxyacetic acid added, g.	26.954	26.954
2.	Initial peroxyacid concentration, %	10.24	10.24
3.	Final peroxyacid concentration, %	1.21	9.47
4.	Correction factor (12/1)	1.069	--
5.	Corrected final peroxyacid concn., %	1.29	9.47
6.	Peroxyacid reacted, % (2-5)	8.95	0.77
7.	Peroxyacid reacted, corrected, %	8.18	
8.	Pure peroxyacid reacted, g. (1 x 7)	2.205	
9.	Pure peroxyacid reacted, mmoles	28.99	
10.	Substrate added, g.	1.849	
11.	Substrate remaining, g. (GLC)	0.315	
12.	Total solution weight, g. (1 + 10)	28.803	
13.	Titer samples withdrawn, g.	2.129	
14.	Difference, g. (12-13)	26.674	
15.	Substrate weight correction (12/14)	1.080	
16.	True substrate remaining, g. (11 x 15)	0.340	
17.	Substrate reacted, g. (10-16)	1.509	
18.	Substrate reacted, mmoles	9.915	
19.	Stoichiometry (9/18)	2.92	
20.	Reaction (17/10), %	81.6	

TABLE LIV

DEGREE OF REACTION FOR STOICHIOMETRY AND PRODUCT YIELDS

Reaction No.	Substrate	Reaction Time, hr.	Substrate Reacted, mmole	Reaction, %	Initial H_2O_2, %
2601- 31-1	4-MC	30	14.84	100	0.63
31-2	4-MC	30	14.87	100	0.63
43-1	4-MC	16	14.59	100	0.86
43-2	4-MC	16	14.60	100	0.86
49-1	4-MC	0.5	13.56	89.2	0.9
49-2	4-MC	0.5	13.94	92.7	0.9
106-1	p-C	6.5	2.57	21.2	0.05
106-2	p-C	16.5	4.86	39.9	0.05
106-3	p-C	26.8	6.24	51.8	0.05
106-4	p-C	40.5	7.34	60.6	0.05
117-1	p-MA	6	1.65	7.5	0.25
117-2	p-MA	16	2.35	19.6	0.25
117-3	p-MA	25	3.02	25.3	0.25
117-4	p-MA	41	4.03	33.1	0.25
144-1	4-MV	3.5	4.65	38.7	0.8
144-2	4-MV	7.5	7.21	59.4	0.8
144-3	4-MV	13	8.51	71.1	0.8
144-4	4-MV	23.5	9.81	80.5	0.8
157-1	4-MV	1	2.15	17.8	1.1
157-2	p-MA	5.8	1.06	8.8	1.1
2629- 90	4-MV	30.5	10.38	86.3	0.03
97	p-MA	74	5.90	47.4	0.1
102	p-C	68	9.63	74.2	0.1
2675- 13-2	4-MV	30	9.92	81.6	0.09
13-4	p-C	57	8.65	71.2	0.09
25-1	p-MA	30	2.83	24.6	0.34
25-2	p-MA	71	5.31	44.0	0.34
25-4	4-MV	30	10.09	84.2	0.34
25-5	4-MC	1.5	12.14	100	0.34
70-1	p-C	48.5	8.19	66.3	0.03
87-1	p-MA	48	3.09	25.5	0.30
87-2	p-MA	72	5.55	45.7	0.30
87-3	4-MV	29	9.96	82.7	0.30
87-4	p-C	54	8.53	70.6	0.30
87-5	4-MC	22	12.05	100	0.30
87-6	4-MC	2	12.02	100	0.30

TABLE LIV (Continued)

DEGREE OF REACTION FOR STOICHIOMETRY AND PRODUCT YIELDS

Reaction No.	Substrate	Reaction Time, hr.	Substrate Reacted, mmole	Reaction, %	Initial H_2O_2, %
2675-128	p-MA	72	6.69	55.5	0.99
155-1	p-MA	72	5.36	44.3	0.05
155-2	4-MV	30	9.78	81.5	0.05
155-3[a]	p-C	54	8.36	69.4	0.05
155-4	o-Q	26	8.21	100	0.05
158	o-Q	0.1	9.01	100	0.05
2617- 55-2[b]	p-Q	50	1.02	36.1	0.05
62-3	M-p-C	24.3	10.31	84.7	0.12
71	p-MA	74.5	5.88	48.7	1.41
80[a,c]	p-C	63	8.61	71.3	0.2
90-3[c]	p-C	56	8.75	72.3	0.28
97[c,d]	4-MC	4	16.20	100	0.3
109[c,d]	4-MC	36	12.10	100	0.5
141[c,d]	4-MC	40	12.10	100	1.0
2668- 87[e]	4-MC	25	12.07	100	1.4

[a] Reaction run in presence of methyl methacrylate.

[b] Initial p-Quinone = 2.82 mm. (0.429 g.); Initial AcO_2H = 7.13%

[c] Remaining peroxyacid not reduced.

[d] Product solution concentrated, not worked up.

[e] Product solution freeze dried.

WORK-UP CONTROLS AND PRODUCT STABILITY

The degree of recovery of known amounts of various substrates and products was determined by running these materials through various stages of the product work-up procedure (see experimental section). The portion of the work-up procedure used in obtaining each result is outlined in Table LVI.

Some p-methylanisole results (resulting from work-up procedure that caused significant loss of p-methylanisole) were corrected to make up for the p-methylanisole lost during work-up. Since the product yields and reaction stoichiometry all depend on the amount of p-methylanisole oxidized, it was important to correct this figure. The work-up control results are in Table LVI. The corrections are shown in Table LV.

TABLE LV

CORRECTIONS FOR p-METHYLANISOLE LOST IN WORK-UP

Reaction No.	Work-Up	p-MA, g.		Correction	p-MA, corrected, g.		Reaction, %
		Initial	Remaining		Remaining	Reacted	
2629- 97	Standard	1.52	0.672	1/0.84	0.800	0.72	47.4
2675- 25-1	Standard	1.407	0.891	1/0.84	1.061	0.346	24.6
25-2	Standard	1.476	0.695	1/0.84	0.827	0.649	44.0
87-1	Standard	1.481	0.927	1/0.84	1.104	0.377	25.5
87-2	Standard	1.483	0.676	1/0.84	0.805	0.678	45.7
128	Direct N_2 Stream	1.473	0.406	1/0.62	0.655	0.818	55.5
155-1	Standard	1.478	0.691	1/0.84	0.823	0.655	44.3
2617- 71	Standard	1.475	0.636	1/0.84	0.757	0.718	48.7

TABLE LVI

WORK-UP CONTROLS

Substrate	Number	Initial Amount Added, g.	Recovery, %	Portion of Work-Up Used
p-Methylanisole	2601-133	1.0135	100.5	Distillation from ether only
	2601-134	0.8860	96.7	Complete (concentration by distillation)
	2675-139	0.8238	62.2	Complete: direct N_2 stream during neutralization
	2675-145	0.6676	71.9	Complete: fed continuously into evaporator; continuous parallel N_2 stream during neutralization
	2675-147-1	0.6162	72.9	Same as 2675-145
	2675-147-2	0.6142	87.9	Concentrated from 350 ml. ether; fed continuously into evaporator; low N_2 flow rate during neutralization
	2675-149	0.6118	96.6	Concentration from 500-ml. flask (rotary evaporator)
	2668-67	0.5170	83.4	Complete: worked up from AcO_2H solution; intermittent N_2 stream during neutralization
	2668-71-2	0.5165	84.5	Same as 2668-67 but no AcO_2H
4-Methylveratrole	2601-135	1.0333	99.7	Complete
	2675-151	0.3234	101+	Concentrated from 250-ml. flask (rotary evaporator)
	2668-69	0.3210	104.7	Complete: from AcO_2H solution
p-Cresol	2629-6	0.8655	100.7	Complete
	2668-71-1	0.3856	99.7	Complete: from AcO_2H solution

TABLE LVI (Continued)

WORK-UP CONTROLS

Substrate	Number	Initial Amount Added, g.	Recovery, %	Portion of Work-Up Used
β-Methyl-lactone	2617-114A	0.6368	84.0	Complete
	2617-150	0.5261	85.6	Complete
2-Me-5-MeO-p-quinone	2617-114E	0.2255	92.5	Complete

β-Methylmuconic acid and the corresponding β-methyl-lactone were dissolved in peroxyacetic acid solution and worked up after certain times. The control reactions run (at 25°) are shown in Table LVII:

TABLE LVII

CONTROL REACTIONS

Reaction No.	Substrate	AcO_2H/H_2O_2, %	Reaction Time, hr.	Material Added, g.
2675-87-7A	β-MMA	5.1/0.15	72	0.100
2668-91-1	β-MMA	6.2/1.5	24	0.101
2668-91-2	β-ML	6.2/1.5	24	0.604
2668-96-2	β-ML	5.0/0.1	24	0.613

The results were discussed in the Results and Discussion section at appropriate times. These results are included in Table LVIII.

TABLE LVIII

PRODUCT STABILITY RESULTS

β-Methylmuconic Acid

2675-87-7A (0.100 g. β-MMA Added)
0.0340 g. Adipic Acid, 100 ml.

Area		Grams
Adipic	β-ML	β-ML
191.8	160.7	0.0470
159.6	129.7	0.0456
208.5	177.4	0.0477
	Average =	0.047

2668-91-1 (0.101 g. β-MMA Added)
0.0222 g. Adipic Acid, 100 ml.

Area		Grams
Adipic	β-ML	β-ML
206.9	181.0	0.0320
205.8	191.3	0.0340
206.0	185.2	0.0329
	Average =	0.033

β-Methyl-Lactone

2668-91-2 (0.604 g. β-ML Added)
0.1011 g. Adipic Acid, 25 ml.

Area		Grams
Adipic	β-ML	β-ML
285.4	172.0	0.1005
283.3	173.2	0.1020
283.6	170.9	0.1005
	Average =	0.1010
	x4 =	0.404

2668-96-2 (0.613 g. β-ML Added)
0.0804 g. Adipic Acid, 25 ml.

Area			Grams	
Adipic	β-ML	β-MMA	β-ML	β-MMA
229.2	172.4	34.1	0.0998	0.0163
250.0	199.0	42.8	0.1056	0.0187
225.4	176.9	38.9	0.1041	0.0189
	Averages =		0.1032	0.0180
	x4 =		0.413	0.072

QUANTITATIVE PRODUCT ANALYSIS

Of all the products in the initial ether extracts of the oxidation solutions, the response factor was known only for the p-quinone (and for the starting material). Therefore, an arbitrary response factor of 1.00 was used for all other products in the ether extract (denoted by the "E" at the end of the reaction number: 2675-87-1E).

Many of the carboxylic acid products in the alkaline layer (denoted by an "A" at the end of the reaction number) also did not have known response factors. However, two were known, and estimates were made as to what the others might be as follows:

Product	Response Factor
γ-Methyl-lactone	1.65 (Estimate)
β-Methyl-lactone	1.65 (Known)
U2	1.60 (Estimate)
U2A	1.60 (Estimate)
β-Methylmuconic acid	1.36 (Known)
U3 + U4	1.36 (Estimate)

The known response factor found for β-methyl-lactone and β-methylmuconic acid were both much above 1.0. It was assumed that the other products would have response factors in this range (1.36-1.65) and thus arbitrarily assuming a response of 1.0 would be inaccurate. Therefore, response factors were chosen based on known similar structures (γ-ML and β-ML) or by similar retention times (β-ML and U2 and U2A; β-MMA and U3 and U4).

Other weight response factors changed from time to time as various columns and conditions were used, and these factors are given with each analysis result. The column and conditions used are also given with each result.

All carboxylic acid products ("A") were analyzed as TMS esters on an SE-30 column at 165° and 75 ml./min. He flow rate. The amount of the 100-ml. solution used (see experimental section) is indicated in parentheses at the end of the reaction number, and the amount of internal standard added is noted just below.

All programming runs were carried out with a 2°/min. temperature increase rate.

The relative amount of methyl esters of the carboxylic acid products was determined as reported in Table LXXV.

Assumptions of product molecular weights had to be made for the unknowns in order to estimate the product yields. The assumed molecular weights of the unknowns were as follows:

Product	Molecular Weight
U1	150
U2	156
U2A	156
U3	156
U4	156
U5	130

The assumptions were based on GLC retention times similar to known compounds. The molecular weight of the compound having the closest retention time to the unknown was rounded off as the unknown molecular weight. The yields of most unknown products were very small, however, so that any error in the assumed molecular weight would not change the results by more than a few percent. The only unknown found to be present in large amounts, U2, was shown by NMR to be very similar to the muconic acid lactones, and thus, the muconic acid molecular weight of 156 was used.

Tables LIX-LXXV use abbreviations in the headings which are explained below:

Abbreviation	Full Name
HO-p-MA	2-Hydroxy-p-methylanisole
Dienone	4-Hydroxy-4-methyl-2,5-cyclohexadienone
p-Quinone or p-Q	2-Methoxy-5-methyl-p-benzoquinone
γ-OH-β-ML	γ-Hydroxy-β-methyl-lactone
γ-ML	γ-Methyl-lactone
β-ML	β-Methyl-lactone
β-MMA	β-Methylmuconic acid
p-C	p-Cresol
p-MA	p-Methylanisole
4-MV	4-Methylveratrole
4-MC	4-Methylpyrocatechol

TABLE LIX

4-METHYLPYROCATECHOL OXIDATION RESULTS[a,b]

2601-49-1 (0.0884 g. p-Methoxyphenol)

Area		Grams
p-MP	4-MC	4-MC
5.95	8.19	1.160
4.41	6.89	0.182
5.69	9.64	0.197
	Average =	0.180

2601-49-2 (0.1190 g. p-Methoxyphenol)

Area		Grams
p-MP	4-MC	4-MC
5.03	4.48	0.140
8.39	5.74	0.107
5.74	4.34	0.118
	Average =	0.121

[a] Run on Apiezon-L, 122°, 120 ml./min., F = 1.31.

[b] All other 4-methylpyrocatechol oxidations went to completion.

TABLE LX

CARBOXYLIC ACID PRODUCTS FROM 4-METHYLPYROCATECHOL

			Area					Grams		
γ-ML	Adipic	β-ML	U2	β-MMA	U3+U4	γ-ML	β-ML	U2	β-MMA	U3+U4
					2675-25-5A (0.2025 g. Adipic Acid, 100 ml.)					
39.7	155.9	317.1	86.3	22.6	34.2	0.0851	0.680	0.179	0.0399	0.0603
32.1	127.0	256.9	71.3	15.0	27.6	0.0845	0.676	0.182	0.0325	0.0598
30.0	125.7	248.4	70.8	19.0	25.8	0.0797	0.660	0.182	0.0416	0.0564
					Averages =	0.083	0.672	0.181	0.038	0.059
					2675-87-5A (0.0516 g. Adipic Acid, 15 ml.)					
38.3	224.0	242.6	37.8	--	20.1	0.0146	0.0922	0.0139	--	0.0063
41.7	226.4	253.7	42.8	--	22.2	0.0157	0.0954	0.0156	--	0.0069
41.7	225.6	258.9	35.3	--	15.3	0.0157	0.0977	0.0129	--	0.0048
					Averages =	0.0153	0.0951	0.0141	--	0.0060
								Correction = 6.667x =		
						0.102	0.634	0.094		0.040
					2617-97 (0.4330 g. Adipic Acid, 100 ml.)					
37.8	247.7	295.5	103.1	55.9	43.9	0.109	0.852	0.288	0.133	0.104
20.4	158.5	181.5	58.0	26.0	23.7	0.092	0.818	0.254	0.097	0.088
34.3	221.8	256.6	92.2	50.7	39.7	0.110	0.827	0.288	0.134	0.105
					Averages =	0.104	0.832	0.277	0.121	0.099

TABLE LX (Continued)

CARBOXYLIC ACID PRODUCTS FROM 4-METHYLPYROCATECHOL

			Area					Grams		
γ-ML	Adipic	β-ML	U2	β-MMA	U3+U4	γ-ML	β-ML	U2	β-MMA	U3+U4
				2617-109 (0.3301 g. Adipic Acid, 100 ml.)						
14.7	230.9	376.4	15.4	7.4	19.0	0.0347	0.888	0.0352	0.0144	0.0369
16.9	212.7	347.9	14.8	6.4	21.5	0.0432	0.891	0.0367	0.0135	0.0453
19.6	210.1	338.5	15.6	4.8	18.0	0.0509	0.878	0.0392	0.0103	0.0385
					Averages =	0.043	0.886	0.037	0.013	0.040
				2617-141 (0.3012 g. Adipic Acid, 100 ml.)						
49.2	263.1	361.1	156.1	29.6	80.5	0.0930	0.682	0.286	0.0461	0.125
41.3	214.1	293.8	133.9	26.7	72.8	0.0959	0.682	0.301	0.0512	0.139
43.3	218.5	296.8	134.0	23.7	72.8	0.0985	0.675	0.296	0.0444	0.136
					Averages =	0.096	0.680	0.294	0.047	0.133
				2668-87 (0.0652 g. Adipic Acid, 20 ml.)						
43.9	248.6	260.9	98.2	25.0	60.8	0.0190	0.1129	0.0412	0.0089	0.0217
40.2	240.3	236.9	88.1	27.3	47.6	0.0180	0.1061	0.0382	0.0101	0.0176
42.1	246.3	244.6	93.0	28.5	59.1	0.0184	0.1069	0.0394	0.0103	0.0213
					Averages =	0.0185	0.1086	0.0396	0.0098	0.0202
							Aliquot correction = 5x =			
						0.093	0.543	0.198	0.049	0.101

TABLE LXI

4-METHYLVERATROLE OXIDATION RESULTS

p-DB	Area 4-MV	Ul	Grams 4-MV	Ul
	2629-90E (0.1020 g. p-Dimethoxybenzene)[a]			
9.45	22.38	1.71	0.255	0.0185
9.29	21.95	1.77	0.254	0.0194
9.91	22.80	1.83	0.248	0.0188
		Averages =	0.252	0.019
	2675-25-4E (0.1900 g. p-Dimethoxybenzene)[b]			
108.2	152.1	34.6	0.285	0.0608
114.6	157.0	35.8	0.278	0.0594
108.1	161.2	41.4	0.303	0.0728
		Averages =	0.289	0.064
	2675-87-3E (0.2028 g. p-Dimethoxybenzene)[c]			
186.8	277.7	21.9	0.322	0.0238
188.5	277.8	21.9	0.319	0.0235
187.8	271.8	21.4	0.313	0.0231
		Averages =	0.318	0.024
	2675-155-2E (0.2232 g. p-Dimethoxybenzene)[c]			
150.6	215.7	17.0	0.342	0.0252
161.5	230.0	18.2	0.340	0.0251
160.2	222.8	17.6	0.332	0.0245
		Averages =	0.338	0.025

[a] Run on Carbowax 20M, 100°, 120 ml./min., F = 1.055.

[b] Run on Carbowax 20M, 100-160°, 120 ml./min., F = 1.068.

[c] Run on Carbowax 20M, 125°, 120 ml./min., F = 1.070.

TABLE LXII

2-METHOXY-5-METHYL-p-BENZOQUINONE
FROM 4-METHYLVERATROLE

Area p-Quinone	Area Internal Standard	Grams p-Quinone
2629-90E (0.1190 g. p-Methoxyphenol)[a]		
193.7	182.1	0.270
234.2	206.5	0.288
227.8	216.6	0.267
	Average =	0.275
2675-25-4E (0.2216 g. p-Methoxyphenol)[a]		
193.4	297.0	0.307
198.4	289.4	0.324
178.8	279.1	0.303
	Average =	0.311
2675-87-3E (0.2450 g. p-Methoxyphenol)[a]		
181.9	477.6	0.199
180.0	483.7	0.194
181.9	478.0	0.199
207.8	521.4	0.208
	Average =	0.200
2675-155-2E (0.1691 g. Trimethoxybenzene)[b]		
175.9	334.0	0.118
167.5	320.1	0.118
188.8	350.1	0.121
	Average =	0.119

[a] Run on Carbowax 20M, 175°, 120 ml./min., F = 2.13.

[b] Run on SE-30, 125°, 75 ml./min., F = 1.33.

TABLE LXIII

CARBOXYLIC ACID PRODUCTS FROM 4-METHYLVERATROLE

			Area					Grams		
γ-ML	Adipic	β-ML	U2	β-MMA	U3+U4	γ-ML	β-ML	U2	β-MMA	U3+U4
					2675-25-4A (0.0327 g. Adipic Acid, 35 ml.)					
17.0	180.7	117.1	120.5	--	25.6	0.0051	0.0350	0.0349	--	0.0063
18.3	191.1	126.7	127.1	--	27.8	0.0052	0.0358	0.0348	--	0.0065
19.7	206.4	137.2	132.2	--	33.8	0.0052	0.0359	0.0335	--	0.0073
					Averages =	0.0052	0.0356	0.0344	--	0.0067
								Correction = 2.857x =		
						0.015	0.102	0.098	--	0.019
					2675-87-3A (0.0212 g. Adipic Acid, 35 ml.)					
34.0	218.3	214.5	114.0	--	39.4	0.0054	0.0344	0.0177	--	0.0052
31.1	191.0	185.8	102.5	--	48.1	0.0057	0.0340	0.0182	--	0.0073
33.6	207.2	205.7	109.5	--	50.8	0.0057	0.0351	0.0179		0.0071
					Averages =	0.0056	0.0345	0.0179	--	0.0065
								Correction = 2.857x =		
						0.016	0.099	0.051	--	0.019

TABLE LXIV

p-CRESOL OXIDATION RESULTS[a]

Area		Grams	Area		Grams
Phenol	p-Cresol	p-Cresol	Phenol	p-Cresol	p-Cresol
2675-13-4E (0.2576 g. Phenol)			2675-87-4E (0.2333 g. Phenol)		
141.6	179.5	0.339	175.6	283.5	0.391
156.1	202.3	0.347	207.5	323.1	0.377
178.2	241.1	0.362	197.0	312.3	0.384
	Average =	0.349		Average =	0.384
2617-80E (0.2967 g. Phenol)			2617-90-3E (0.3051 g. Phenol)		
259.9	314.7	0.373	207.9	234.9	0.358
243.6	293.5	0.371	195.1	219.4	0.356
221.4	274.8	0.382	202.2	236.6	0.371
	Average =	0.375		Average =	0.362

[a]Run on Carbowax 20M, 150°, 120 ml./min., F = 1.038.

TABLE LXV

NEUTRAL PRODUCTS FROM p-CRESOL

Internal Standard	Area Acetal	Dienone	U5	Grams Acetal	Dienone	U5
			2675-13-4E (0.1140 g. p-Dimethoxybenzene)[a]			
201.1	29.0	124.2	12.0	0.0164	0.0704	0.0068
198.0	28.4	122.9	13.0	0.0164	0.0708	0.0075
186.1	27.5	115.2	10.3	010168	0.0706	0.0063
			Averages =	0.017	0.071	0.007
			2675-87-4E (0.2333 g. Phenol)[b]			
175.6	133.1	17.9	4.6	0.177	0.0238	0.0061
207.5	155.2	21.1	7.0	0.174	0.0237	0.0079
197.0	145.4	20.7	5.0	0.172	0.0245	0.0059
			Averages =	0.174	0.024	0.007
			2617-80E (0.2967 g. Phenol)[b]			
259.9	--	95.2	14.5	--	0.109	0.0166
243.6	--	90.1	12.4	--	0.110	0.0151
221.4	--	82.1	9.8	--	0.110	0.0132
			Averages =	--	0.110	0.015
			2617-90-3E (0.3051 g. Phenol)[b]			
207.9	--	34.5	4.6	--	0.0506	0.0067
195.1	--	34.2	3.9	--	0.0535	0.0061
202.2	--	33.8	3.5	--	0.0511	0.0053
			Averages =	--	0.052	0.006

[a] Run on Carbowax 20M, 100-160°, 120 ml./min., F = 1.00.

[b] Run on Carbowax 20M, 150°, 120 ml./min., F = 1.00.

TABLE LXVI

CARBOXYLIC ACID PRODUCTS FROM p-CRESOL

Area						Grams				
γ-ML	Adipic	β-ML	U2	β-MMA	U3+U4	γ-ML	β-ML	U2	β-MMA	U3+U4
					2675-13-4A (0.1961 g. Adipic Acid, 100 ml.)					
23.9	253.4	249.9	108.3	--	37.9	0.031	0.319	0.134	--	0.0396
25.7	261.7	256.2	117.0	--	46.2	0.032	0.317	0.140	--	0.0467
25.6	257.7	254.7	118.4	--	47.2	0.032	0.320	0.144	--	0.0485
					Averages =	0.032	0.319	0.139	--	0.0449
								Correction = 1.082x =		
						0.035	0.345	0.150	--	0.049
					2675-87-4A (0.1549 g. Adipic Acid, 100 ml.)					
28.6	231.9	194.3	112.2	--	--	0.0316	0.214	0.120	--	--
26.8	214.9	176.9	100.2	--	12.4	0.0319	0.210	0.116	--	0.0122
29.7	222.3	190.8	114.2	--	18.6	0.0342	0.219	0.127	--	0.0177
					Averages =	0.033	0.214	0.121	--	0.015
					2617-80A (0.0415 g. Adipic Acid, 25 ml.)					
26.2	202.7	172.1	31.4	6.5	--	0.0089	0.0582	0.0103	0.0018	--
27.8	208.0	185.2	26.3	6.9	--	0.0092	0.0610	0.0084	0.0019	--
23.2	194.2	156.3	25.6	6.0	--	0.0082	0.0551	0.0088	0.0017	--
					Averages =	0.0088	0.0581	0.0092	0.0018	--
								Aliquot correction = 4x =		
						0.035	0.232	0.037	0.007	--
					2617-90-3A (0.0350 g. Adipic Acid, 25 ml.)					
39.0	239.4	263.3	113.1	5.6	71.4	0.0094	0.0635	0.0265	0.0011	0.0142
32.9	209.2	227.7	99.6	7.2	71.1	0.0091	0.0629	0.0267	0.0016	0.0162
32.1	199.3	215.6	94.0	10.5	67.8	0.0093	0.0625	0.0264	0.0025	0.0162
					Averages =	0.0093	0.0630	0.0265	0.0017	0.0155
								Aliquot correction = 4x =		
						0.037	0.252	0.106	0.007	0.062

TABLE LXVII

p-METHYLANISOLE OXIDATION RESULTS[a]

Area Anisole	Area p-MA	Grams p-MA
2675-25-1E (0.810 g. Anisole)		
223.0	238.2	0.883
242.3	259.7	0.886
251.4	271.8	0.894
253.9	276.7	0.901
	Average =	0.891
2675-87-1E (0.932 g. Anisole)		
121.8	118.8	0.928
149.2	148.5	0.947
166.1	159.6	0.914
160.4	154.9	0.919
	Average =	0.927
2675-128E (0.612 g. Anisole)		
214.5	134.1	0.391
204.1	127.7	0.391
207.7	129.5	0.390
	Average =	0.391
2617-71E (0.5090 g. Anisole)		
167.9	198.4	0.614
143.6	167.7	0.607
135.7	160.4	0.614
	Average =	0.612
2675-25-2E (0.499 g. Anisole)		
249.9	352.2	0.718
243.4	324.6	0.680
203.4	275.2	0.689
200.9	273.9	0.695
	Average =	0.695
2675-87-2E (0.674 g. Anisole)		
177.8	173.6	0.672
172.6	173.0	0.690
179.4	173.3	0.665
	Average =	0.676
2675-155-1E (0.334 g. Anisole)		
99.7	193.2	0.661
108.2	211.5	0.667
89.3	174.3	0.666
	Average =	0.665

[a] Run on Carbowax 20M, 70°, 120 ml./min., $\underline{F}$ = 1.021.

TABLE LXVIII

NEUTRAL PRODUCTS FROM p-METHYLANISOLE[a]

	Area				Grams			
p-DB	Acetal	HO-p-MA	Dienone	U7	Acetal	HO-p-MA	Dienone	U7
			2675-25-1E (0.0971 g. p-Dimethoxybenzene)					
182.0	190.5	41.5	10.1	--	0.102	0.0221	0.0054	--
183.2	197.2	42.7	10.7	--	0.105	0.0226	0.0057	--
179.0	202.1	40.0	16.0	--	0.110	0.0217	0.0087	--
95.0	105.5	20.1	--	--	0.108	0.0205	--	--
				Averages =	0.106	0.022	0.007	--
			2675-25-1E (0.0940 g. p-Dimethoxybenzene)					
134.0	175.5	18.0	5.4	11.5	0.123	0.0126	0.0038	0.0079
153.9	194.5	19.2	5.8	12.9	0.119	0.0117	0.0035	0.0079
143.3	185.2	17.0	8.4	13.5	0.122	0.0112	0.0055	0.0089
147.8	188.5	18.5	6.0	13.4	0.120	0.0118	0.0038	0.0085
				Averages =	0.121	0.012	0.004	0.008
			2675-87-1E (0.0943 g. p-Dimethoxybenzene)					
212.6	181.2	56.5	40.2	7.4	0.0804	0.0251	0.0178	0.0033
182.3	150.0	49.0	34.6	7.1	0.0776	0.0253	0.0179	0.0037
170.9	142.3	58.0	30.7	6.4	0.0785	0.0320	0.0169	0.0035
				Averages =	0.079	0.028	0.018	0.004
			2675-87-2E (0.1067 g. p-Dimethoxybenzene)					
217.6	189.4	34.8	67.5	21.8	0.0929	0.0170	0.0330	0.0107
227.8	209.9	42.5	74.1	25.8	0.0983	0.0199	0.0347	0.0121
224.4	206.7	39.9	70.7	26.5	0.0983	0.0190	0.0337	0.0126
				Averages =	0.096	0.019	0.034	0.012
			2675-155-1E (0.1007 g. p-Dimethoxybenzene)					
78.4	107.3	13.6	11.4	7.7	0.138	0.0175	0.0146	0.0099
164.3	226.3	32.3	27.1	19.8	0.139	0.0198	0.0166	0.0121
128.1	172.6	24.2	18.4	17.9	0.137	0.0190	0.0145	0.0141
				Averages =	0.138	0.0188	0.0152	0.0120
						Correction =	1.041x =	
					0.144	0.020	0.016	0.012

TABLE LXVIII (Continued)

NEUTRAL PRODUCTS FROM p-METHYLANISOLE[a]

		Area				Grams		
p-DB	Acetal	HO-p-MA	Dienone	U7	Acetal	HO-p-MA	Dienone	U7
			2617-71E (0.1070 g. p-Dimethoxybenzene)					
127.1	145.6	19.6	46.6	18.8	0.123	0.0165	0.0393	0.0158
140.7	157.7	23.7	51.8	20.3	0.120	0.0180	0.0393	0.0154
123.7	132.8	19.2	45.3	18.4	0.115	0.0166	0.0391	0.0159
				Averages =	0.119	0.0170	0.0392	0.0157
						Correction =	1.040x =	
					0.124	0.018	0.041	0.016

[a]Run on Carbowax 20M, 100-160°, 120 ml./min., F = 1.00.

TABLE LXIX

2-METHOXY-5-METHYL-o-BENZOQUINONE
FROM p-METHYLANISOLE

Area		Grams
p-Quinone	Internal Standard	p-Quinone
2675-25-2E (0.1200 g. p-Methoxyphenol)[a]		
192.5	330.9	0.149
189.6	330.4	0.147
193.4	327.1	0.151
	Average =	0.149
2675-87-2E (0.0461 g. p-Methoxyphenol)[a]		
195.7	287.6	0.0668
226.5	331.4	0.0671
243.9	349.1	0.0686
248.4	356.4	0.0684
	Average =	0.068
2675-128E (0.186 g. Trimethoxybenzene)[b]		
215.1	355.5	0.150
229.3	381.3	0.149
214.4	360.1	0.147
	Average =	0.149 x 1.040 = 0.155
2675-155-1E (0.2286 g. Trimethoxybenzene)[b]		
91.1	341.3	0.0811
106.4	349.9	0.0924
124.8	394.7	0.0961
	Average =	0.0899 x 1.041 = 0.094
2617-71E (0.2118 g. Trimethoxybenzene)[b]		
95.8	273.6	0.0986
119.4	346.1	0.0972
111.1	338.2	0.0925
	Average =	0.0961 x 1.040 = 0.100

[a] Run on Carbowax 20M, 175°, 120 ml./min., F = 2.13.

[b] Run on SE-30, 125°, 75 ml./min., F = 1.33.

TABLE LXX

CARBOXYLIC ACID PRODUCTS FROM p-METHYLANISOLE

Area						Grams				
γ-ML	Adipic	β-ML	U2	β-MMA	U3+U4	γ-ML	β-ML	U2	β-MMA	U3+U4
					2675-25-1A (0.0390 g. Adipic Acid, 100 ml.)					
16.8	249.8	107.4	51.1	--	15.4	0.0043	0.0277	0.0128	--	0.0033
16.1	257.4	106.9	53.2	--	14.8	0.0040	0.0267	0.0129	--	0.0031
15.1	252.4	107.1	56.3	--	13.9	0.0038	0.0273	0.0139	--	0.0029
					Averages =	0.004	0.027	0.013	--	0.003
					2675-25-2A (0.0320 g. Adipic Acid, 100 ml.)					
29.4	161.1	184.4	117.4	3.5	96.6	0.0096	0.0604	0.0373	0.0009	0.0261
30.5	165.7	200.8	122.8	3.4	104.1	0.0097	0.0640	0.0379	0.0009	0.0273
31.0	162.5	192.8	124.4	7.0	112.7	0.0101	0.0626	0.0392	0.0019	0.0302
					Averages =	0.010	0.062	0.038	0.001	0.028
					2675-87-1A (0.0409 g. Adipic Acid, 100 ml.)					
19.0	261.3	129.8	50.9	--	46.0	0.0049	0.0335	0.0128	--	0.0098
17.5	234.8	118.5	46.2	--	41.4	0.0050	0.0341	0.0129	--	0.0098
19.5	262.9	131.8	49.8	--	44.5	0.0050	0.0338	0.0124	--	0.0094
					Averages =	0.005	0.034	0.013	--	0.001

TABLE LXX (Continued)

CARBOXYLIC ACID PRODUCTS FROM p-METHYLANISOLE

Area						Grams				
γ-ML	Adipic	β-ML	U2	β-MMA	U3+U4	γ-ML	β-ML	U2	β-MMA	U3+U4
				2675-87-2A (0.0207 g. Adipic Acid, 50 ml.)						
26.4	220.5	198.7	93.3	12.1	61.2	0.0041	0.0308	0.0140	0.0015	0.0078
20.5	185.8	163.5	81.2	9.9	51.8	0.0038	0.0310	0.0145	0.0015	0.0078
22.2	193.3	174.8	82.2	10.7	50.4	0.0039	0.0309	0.0141	0.0016	0.0073
					Averages =	0.0039	0.0306	0.0142	0.0015	0.0076
						Aliquot correction = 2x =				
						0.008	0.061	0.028	0.003	0.015
				2675-128A (0.0109 g. Adipic Acid, 100 ml.)						
3.7	222.6	2.5	102.9	--	--	--	--	0.0080	--	--
3.8	213.0	2.3	98.9	--	--	--	--	0.0081	--	--
3.6	198.8	2.8	92.3	--	--	--	--	0.0081	--	--
					Averages =	--	--	0.0081	--	--
								Correction = 1.040x =		
						--	--	0.008	--	--
				2617-71A (0.0118 g. Adipic Acid, 100 ml.)						
7.7	91.2	8.7	86.1	--	--	0.002	0.002	0.0178	--	--
8.0	94.5	10.0	94.4	--	--	0.002	0.002	0.0189	--	--
9.9	100.4	9.6	93.3	--	--	0.002	0.002	0.0176	--	--
					Averages =	0.002	0.002	0.0181	--	--
								Correction = 1.040x =		
						0.002	0.002	0.019	--	--

TABLE LXXI

2-METHOXY-5-METHYL-p-BENZOQUINONE OXIDATION RESULTS

Area p-Quinone	Area Internal Standard	Grams p-Quinone
2629-130E (0.1750 g. p-Methoxyphenol)[a]		
107.2	317.2	0.106
102.8	366.9	0.104
91.0	345.7	0.099
	Average =	0.103
2617-55-2 (0.2671 g. Trimethoxybenzene)[b]		
277.3	377.0	0.261
274.5	350.9	0.278
302.4	432.5	0.248
	Average =	0.263

[a]Run on Carbowax 20M, 175°, 120 ml./min., F = 2.13.

[b]Run on SE-30, 125°, 75 ml./min., F = 1.33.

TABLE LXXII

2-METHOXY-p-CRESOL OXIDATION RESULTS

Area Guaiacol	Area MeO-Cresol	Grams MeO-Cresol
2617-62-3E (0.2010 g. Guaiacol)[a]		
128.7	140.7	0.235
176.2	202.6	0.247
194.9	235.3	0.260
	Average =	0.247 x 1.040 = 0.257

[a]Run on Carbowax 20M, 140°, 120 ml./min., F = 1.07.

TABLE LXXIII

CARBOXYLIC ACID PRODUCTS FROM 2-METHOXY-p-CRESOL

Area						Grams				
γ-ML	Adipic	β-ML	U2	β-MMA	U3+U4	γ-ML	β-ML	U2	β-MMA	U3+U4
2617-62-3A (0.0349 g. Adipic Acid, 20 ml.)										
19.7	239.6	121.6	87.9	8.5	28.4	0.0047	0.0292	0.0205	0.0017	0.0056
20.0	228.6	111.3	81.7	4.4	23.7	0.0050	0.0280	0.0199	0.0009	0.0049
23.7	233.3	123.9	88.4	6.5	29.5	0.0059	0.0306	0.0211	0.0013	0.0060
					Averages =	0.0052	0.0293	0.0205	0.0013	0.0055
					Aliquot correction x correction = 5 x 1.04 = 5.2x =	0.027	0.152	0.107	0.007	0.029

TABLE LXXIV

CARBOXYLIC ACID PRODUCTS FROM 4-METHYL-o-BENZOQUINONE

		Area				Grams				
γ-ML	Adipic	β-ML	U2	β-MMA	U3+U4	γ-ML	β-ML	U2	β-MMA	U3+U4
				2675-155-4A (0.2011 g. Adipic Acid, 100 ml.)						
43.3	254.7	322.2	122.2	27.3	47.0	0.0564	0.420	0.154	0.0292	0.0503
43.5	258.1	318.5	112.2	30.0	37.9	0.0560	0.409	0.140	0.0317	0.0401
49.8	292.9	373.8	131.2	30.2	51.6	0.0564	0.423	0.144	0.0281	0.0481
					Averages =	0.056	0.417	0.146	0.030	0.046
				2675-158A (0.0485 g. Adipic Acid, 20 ml.)						
39.3	150.2	223.5	--	10.3	--	0.0209	0.1191	--	0.0045	--
39.4	144.8	228.3	--	12.0	--	0.0218	0.1262	--	0.0055	--
42.1	153.0	241.4	--	13.0	--	0.0220	0.1263	--	0.0056	--
					Averages =	0.0216	0.1239	--	0.0052	--
					Aliquot correction = 5x =	0.108	0.620	--	0.026	--

TABLE LXXV

RELATIVE YIELDS OF METHYL ESTERS OF CARBOXYLIC ACID PRODUCTS[a]

	Area	%	Fraction	Area	%	Fraction
	2629-90A (4-MV)			2629-97A (p-MA)		
γ-ML	3.7	11	0.14	3.6	11	0.16
γ-OH-β-ML	4.8	14	0.19	6.1	19	0.27
β-ML	25.6	75	1.00	23.0	70	1.00
Total	34.1	100		32.7	100	
	2629-102A (p-Cresol)			2629-113A (4-MC)		
γ-ML	3.7	13	0.18	4.8	24	0.37
γ-OH-β-ML	4.5	16	0.22	1.8	9	0.14
β-ML	20.2	71	1.00	13.1	67	1.00
Total	28.4	100		19.7	100	
	2668-102 (o-Quinone)			2668-96-1 (2-MeO-p-Cresol)		
γ-ML	122	16	0.19	44	7	0.19
γ-OH-β-ML	0	0	0	337	55	1.43
β-ML	639	84	1.00	235	38	1.00
Total	761	100		616	100	

[a]Run on Carbowax 20M, 185°, 120 ml./min.